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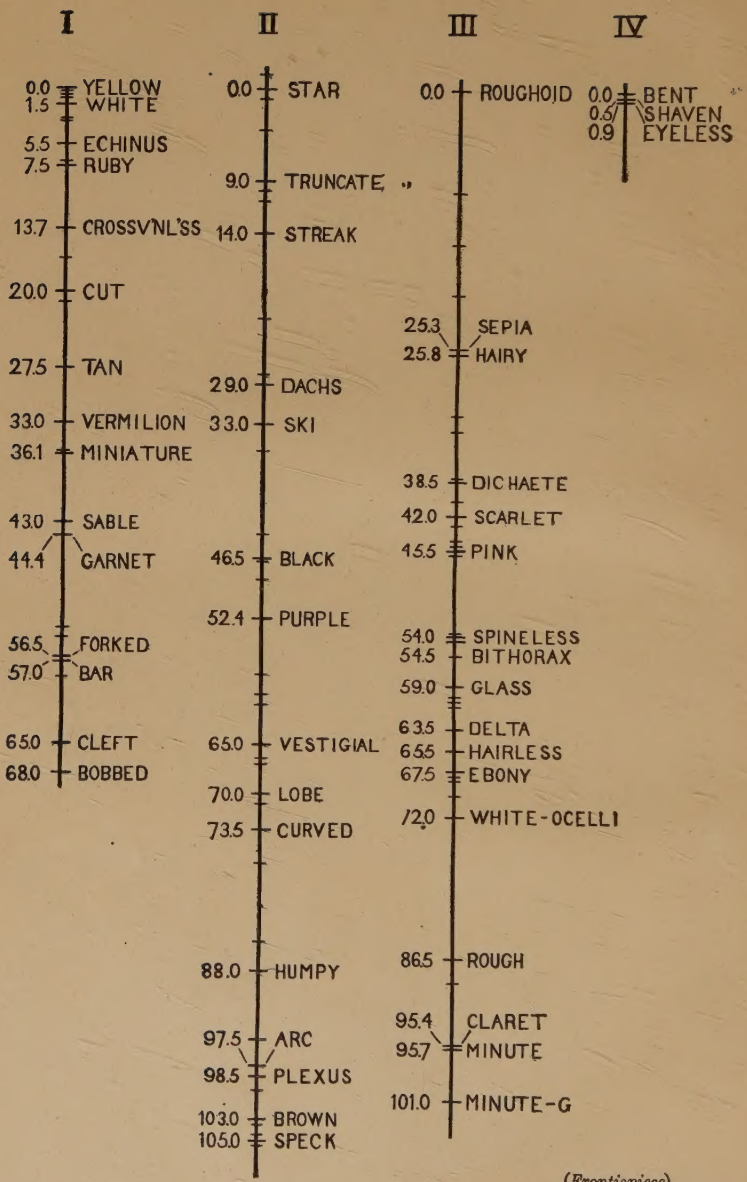
THE MECHANISM

OF

MENDELIAN HEREDITY



(*Frontispiece*)

THE MECHANISM
OF
MENDELIAN HEREDITY

BY

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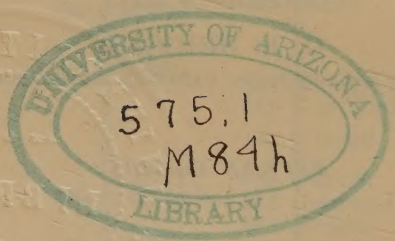

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To

EDMUND BEECHER WILSON

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PREFACE

From ancient times heredity has been looked upon as one of the central problems of biological philosophy. It is true that this interest was largely speculative rather than empirical. But since Mendel's discovery of the fundamental law of heredity in 1865, or rather since its re-discovery in 1900, a curious situation has begun to develop. The students of heredity calling themselves geneticists have begun to draw away from the traditional fields of zoology and botany, and have concentrated their attention on the study of Mendel's principles and their later developments. The results of these investigators appear largely in special journals. Their terminology is often regarded by other zoologists as something barbarous,—outside the ordinary routine of their profession. The tendency is to regard genetics as a subject for specialists instead of an all-important theme of zoology and botany. No doubt this is but a passing phase; for biologists can little afford to hand over to a special group of investigators a part of their field that is and always will be of vital import. It would be as unfortunate for all biologists to remain ignorant of the modern advances in the study of heredity as it would be for the geneticists to remain unconcerned

as to the value for their own work of many special fields of biological inquiry. What is fundamental in zoology and botany is not so extensive, or so intrinsically difficult, that a man equipped for his profession should not be able to compass it.

In the following pages we have attempted to separate those questions that seem to us significant from that which is special or merely technical. We have, of course, put our own interpretation on the facts, and while this may not be agreed to on all sides, yet we believe that in what is essential we have not departed from the point of view that is held by many of our co-workers at the present time. Exception may perhaps be taken to the emphasis we have laid on the chromosomes as the material basis of inheritance. Whether we are right here, the future—probably a very near future—will decide. But it should not pass unnoticed that even if the chromosome theory be denied, there is no result dealt with in the following pages that may not be treated independently of the chromosomes; for, we have made no assumption concerning heredity that cannot also be made abstractly without the chromosomes as bearers of the postulated hereditary factors. Why then, we are often asked, do you drag in the chromosomes? Our answer is that since the chromosomes furnish exactly the kind of mechanism that the Mendelian laws call for; and since there is an ever-increasing body of information that points clearly to the chromosomes as the bearers of the

Mendelian factors, it would be folly to close one's eyes to so patent a relation. Moreover, as biologists, we are interested in heredity not primarily as a mathematical formulation but rather as a problem concerning the cell, the egg, and the sperm.

T. H. M.

PREFACE TO SECOND EDITION

We have tried to bring the book up to date not only by adding here and there throughout the text the latest results on the subject, but also by adding two entirely new chapters, and new maps of the best known mutant factors. Much new material has been added to the chapter on sex; the chapter on selection has been largely rewritten. The new chapters are one on heredity in Protozoa, and one on mutation in the evening primrose. In the latter field, the latest results of de Vries and others on Oenothera, and the work on balanced lethals, bid fair to bring the earlier discoveries of de Vries into line with more recent work in the whole field of mutation and inheritance.

In place of the "Appendix" we have prepared a small manual for laboratory use (Henry Holt and Co., Publishers) that gives directions for carrying out genetic experiments with the pomace fly. These experiments have been picked out as the ones most

suitable for student work, and also because they serve to illustrate, in a practical way, most of the fundamental principles of heredity. In addition, the newest culture methods for breeding Drosophila are given, as well as other methods of handling this material.

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THE MECHANISM OF MENDELIAN HEREDITY

CHAPTER I

MENDELIAN INHERITANCE AND THE CHROMOSOMES

Mendel's fundamental law of segregation was announced in 1865. It is very simple. *The units contributed by each parent separate in the germ cells of the offspring without having had any influence on each other.* For example, in a cross between yellow-seeded and green-seeded peas, one parent contributes to the offspring a unit for yellow and the other parent contributes a unit for green. These units separate in the ripening of the germ cells of the offspring so that half of the germ cells are yellow producing and half are green producing. This separation occurs both in the eggs and in the pollen.

Mendel did not know of any mechanism by which such a process could take place. In fact, in 1865 very little was known about the ripening of the germ cells. But in 1900, when Mendel's long-forgotten discovery was brought to light once more, a mechanism had been discovered that fulfils exactly the Mendelian requirements of pairing and separation.

The sperm of every species of animal or plant

carries a definite number of bodies called chromosomes. The egg carries the same number. Consequently, when the sperm unites with the egg, the fertilized egg will contain the double number of chromosomes. For each chromosome contributed by the sperm there is a corresponding chromosome contributed by the egg, *i.e.*, there are two chromosomes of each kind, which constitute a pair (Fig. 1, *a*).

When the fertilized egg divides, every chromosome splits into two chromosomes, and these two daughter chromosomes then move apart, going to opposite poles of the dividing cell (Fig. 1, *c*). Thus each daughter cell (Fig. 1, *d*) receives one of the daughter chromosomes formed from each original chromosome. The same process occurs in all cell divisions, so that all the cells of the animal or plant come to contain the double set of chromosomes.

The germ cells also have at first the double set of chromosomes, but when they are ready to go through the last stages of their transformation into sperm or eggs the chromosomes unite in pairs (Fig. 1, *e*). Then follows a different kind of division (Fig. 1, *f*) at which the chromosomes do not split but the members of each pair of chromosomes separate and each member goes into one of the daughter cells (Fig. 1, *g*, *h*). As a result each mature germ cell receives one or the other member of every pair of chromosomes and the number is reduced to half. Thus the behavior of the chromosomes parallels the behavior of the Mendelian units, for in the germ cells each unit derived from the father separates from the

corresponding unit derived from the mother. These units will henceforth be spoken of as factors; the two factors of a pair are called allelomorphs of each

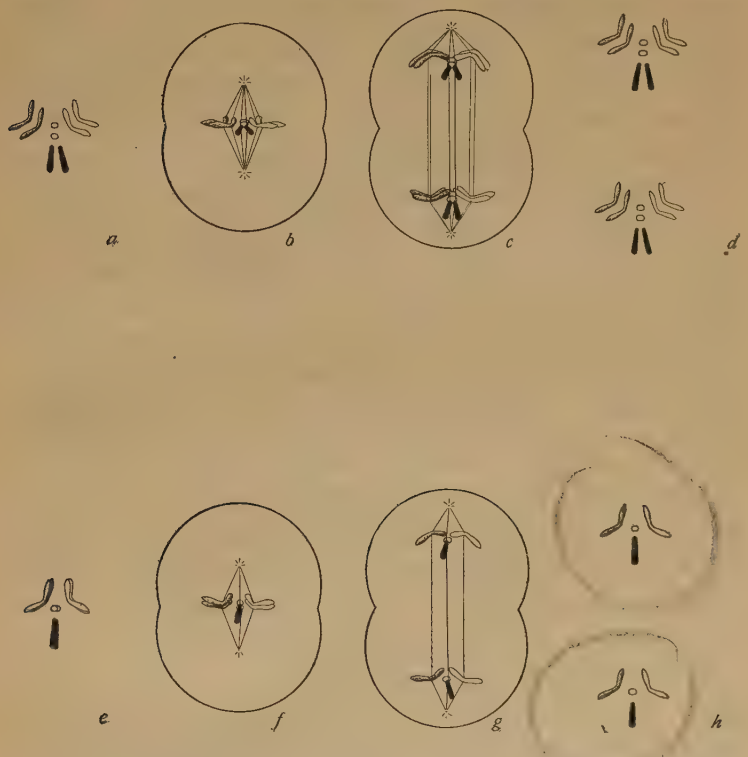


FIG. 1.—In the upper line, four stages in the division of the egg (or of a body cell) are represented. Every chromosome divides when the cell divides. In the lower line the "reduction division" of a germ cell, after the chromosomes have united in pairs, is represented. The members of each of the four pairs of chromosomes separate from each other at this division.

other. Their separation in the germ cells is called segregation.

The possibility of explaining Mendelian phenomena

by means of the manœuvers of the chromosomes seems to have occurred to more than one person, but W. Sutton (1902) first presented the idea in the form in which we recognize it today. Moreover, he not only called attention to the fact above mentioned, that both chromosomes and hereditary factors undergo segregation, but showed that if the pairs assort independently, Mendel's second law ("assortment") is fulfilled. Mendel had found that when the inheritance of more than one pair of factors is followed, the different pairs of factors sort out independently of one another. Thus in a cross of a pea having both green seeds and tall stature with a pea having yellow seeds and short stature, the fact that a germ cell receives a particular member of one pair (*e.g.*, yellow) does not determine which member of the other pair it receives; it is as likely to receive the tall as the short. Sutton pointed out that in the same way the segregation of one pair of chromosomes is probably independent of the segregation of the other pairs.

It was obvious from the beginning, however, that there was one essential requirement of the chromosome view, namely, that all the factors carried by the *same* chromosome should tend to remain together. Therefore, since the number of inheritable characters may be large in comparison with the number of pairs of chromosomes, we should expect actually to find not only the independent behavior of pairs, but also cases in which characters are linked together in groups in their inheritance. Even in species where a limited

number of Mendelian units are known, we should still expect to find some of them in groups.

In 1906 Bateson and Punnett made the discovery of linkage, which they called gametic coupling. They found that when a sweet pea with factors for purple flowers and long pollen grains was crossed to a pea with factors for red flowers and round pollen grains, the two factors that came from the same parent tended to be inherited together. Here was the first case that gave the sort of result that was to be expected if factors were in chromosomes, although this relation was not pointed out at the time. In the same year, however, Lock called attention to the possible relation between the chromosome hypothesis and linkage.

In other groups a few cases of coupling became known, but nowhere had the evidence been sufficiently ample or sufficiently studied to show how frequently coupling occurs. Since 1910, however, in the fruit fly, Drosophila melanogaster, a large number of new characters have appeared by mutation, and so rapidly does the animal reproduce that in a relatively short time the inheritance of more than a hundred characters has been studied. It became evident very soon that these characters are inherited in groups. There is one great group of characters that are sex linked. There are two other groups of characters slightly greater in number. Finally a character appeared that did not belong to any of the other groups, and a year later still another character appeared that was linked to the last one but was independent of all the

other groups. Hence in Drosophila there are four groups of characters, a partial list of which follows:

GROUP I

Abnormal, A
Bar, B
Bar–def'y
bifid, bi
blood, w^b
bordered, bd
broad, br
buff, w^{bf}
cherry, w^c
cleft, cf
club, cl
crooked, fw^c
crossv'less, cv
cut, ct
cut^3, ct^3
cut^6, ct^6
depressed
double
dusky, dy
dusky^2, dy^2
echinus, ec
écru, w^{ec}
eosin, w^e
facet, fa
forked, f
furrowed, fw
fused, fu
garnet, g
garnet^2, g^2
ivory, w^i
lemon
lethals (50)
lozenge, lz
lozenge^2, lz^2
miniature, m
Notch, N (18)
prune, pn
roughish, rh
ruby, rb
ruby^2, rb^2
rudimentary, r
rud'y^7, r^7
sable, s
Sable–dup.
scute, sc
short, br^s
singed, sn
small-eye, sy
small-w'g, sl
spot, y^s
tan, t
tiny-br', tb
tinged, w^t
vermilion, v
Verm.–def'y
Verm.–dup.
white, w
yellow, y

GROUP II

abrupt
amethyst
antlered, vg^a
apterous, ap
arc, a
aristaless, al
balloon, ba
black, b
blistered, bs
brown, bw
chubby
cinnabar, cn
Confluent, Cf.
Cream–II
cream–b
cream–c
CIIL
CIIR
CIIS
Curly, Cy
curved, c
dachs, d
Dachs–def'y
dachsoid
dachsous
dash
Detached
expanded, ex
flipper, fp
fringed, fr
gap-vein
Gull, G
humpy, hy
jaunty, j
lethals (9)
Lobe, L
Lobe^2, L^2
Minute–b
Minute–dII
Minute–e
morula, mr
narrow, nw
nick, vg^n
oblique
olive
pads
Pale–II, PII
patched
pinkish
Plus–mod.–D
pink-wing, pw
purple, pr
purploid, pd
reduced, rd
roof
safranin, sf
scraggly, rd^s
Ski–II, Si
sienna, pr^s
Snub, T^s
square, T^{sq}
speck, sp
Star, S
strap, vg^s
straw, sw
Streak, Sk
telegraph, tg
telescope, ts
translucent, tl
trefoil, tf
Truncate, T
vortex, T^v
yellowish

GROUP III

ascute, as
band, bn
Beaded, Bd
benign-tumor
bithorax, bx
bithorax–b
cardinal, cd
claret, ca
cream–III
compressed
curled, cu
CIII
CIII, II
CIIIP
Deformed, Df
Delta, Δ
Dichæte, D
dilute
divergent, dv
dwarf, dw
dwarf–b
ebony, e
ebony^4, e^4
Extended, DE
giant, gt
glass, gl
Hairless, H
hairy, h
Intensifier–BD
Intensifier–S
Intensifier–T
kidney, k
lethals (9)
mahogany
maroon, ma
Minute, M
Minute–dIII
Minute–f
Minute–g
olive–III
Pale–III, PIII
peach, pp
pink, p
Pointed-wing
Roof–c
rotated–abd.
rough, ro
roughoid, ru
safranin–b
scarlet, st
sepia, se
ski–III, si
smudge
sooty, e^s
spineless, ss
spread, sd
tilt, tt
tumor, tu
Two-bristles
varnished, vr
vortex–III
warped, wp
white-ocelli, wo
with

GROUP IV

bent, bt
bent^2, bt^2
eyeless, ey
eyeless^2, ey^2
shaven, sv

The four pairs of chromosomes of the female of Drosophila are shown in Fig. 2 (to the left). There are three pairs of large chromosomes and one pair of small chromosomes. One of the four pairs is the pair of sex or X chromosomes. In the male, Fig. 2 (to the right), there are likewise three pairs of large chromosomes and a smaller pair. The two sex chromosomes in the male have been found to be dis-

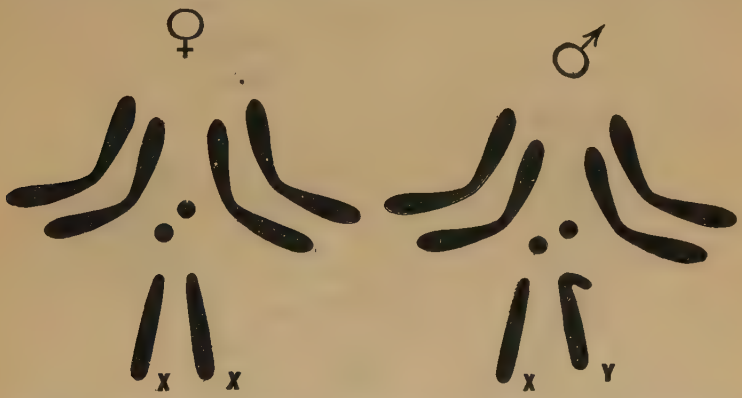


FIG. 2.— Diagram of female and of male group (duplex) of chromosomes of Drosophila melanogaster showing the four pairs of chromosomes. The hook on the Y chromosome is characteristic. The members of each pair are usually found together, as here.

tinguishable from each other in shape. This distinction was first observed in the oögonial figures of the XXY females that had arisen through non-disjunction. Satisfactory figures of the spermatogonial groups were much more difficult to obtain, but these also showed that the Y was J-shaped and somewhat longer than the X. In length the chromosomes are in the ratio: X = 100: Y = 112: II = 159: III = 159: IV = 12. Stevens' work had seemed to show

that the X chromosome is attached to another chromosome and that there is no Y chromosome. In the earlier papers on Drosophila this relation of the chromosomes was assumed to be correct and the female was represented as XX and the male as XO.

In Drosophila, then, there is a numerical correspondence between the number of hereditary groups and the number of the chromosomes. Moreover, the size relations of the groups and of the chromosomes correspond. The method of inheritance of the factors carried by these chromosomes will now be considered more in detail.

The Inheritance of one Pair of Factors

The inheritance of a single pair of characters may be illustrated by the following examples from Drosophila, one from each of the four groups.

The mutant stock called vestigial is so characterized because it has only small vestiges of the wings. If a fly with vestigial wings is mated to the wild type with long wings (Fig. 3, P_1), the offspring will have long wings (Fig. 3, F_1). If these hybrid flies of the first generation (the first filial generation, or F_1) are mated to each other, their offspring (or F_2) will be of two sorts: some will have long wings and others will have vestigial wings. There will be three times as many flies with long wings as flies with vestigial wings. This is the Mendelian ratio of 3:1 that appears when a single pair of characters is involved.

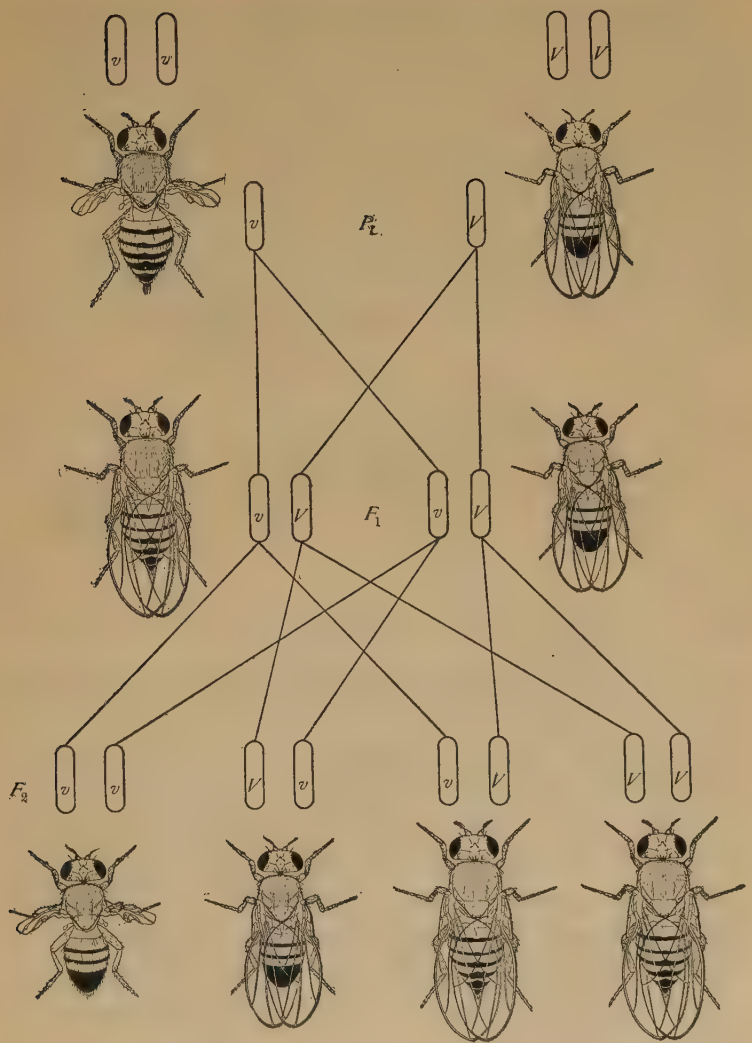


FIG. 3.—Vestigial winged by long winged (wild-type) fly. The second chromosome that carries the recessive factor for vestigial is here represented by the oval containing the letter v. The "normal" second chromosome contains here the capital letter V.

If the factors for vestigial wings are carried by a pair of chromosomes (the chromosomes carrying v in Fig. 3) then at the ripening of the germ cells (eggs and sperm) such a pair of chromosomes will come together and at reduction separate; so that each germ cell will have one such chromosome and not the other. (See Fig. 1, *e–h.*)

If such a germ cell fertilizes an egg of the wild fly that contains a similar group of chromosomes, ex-

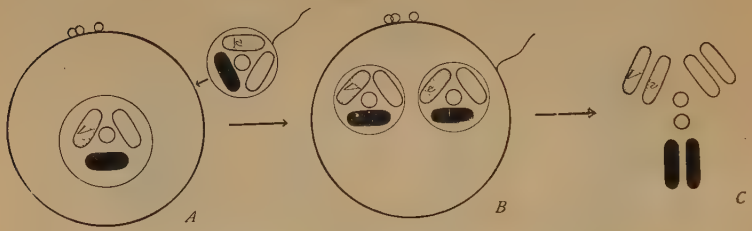


FIG. 4.—(*A.*) Fertilization of egg by sperm. (*B.*) Zygote formed by union of egg and sperm. (*C.*) Diploid nucleus.

cept that the corresponding chromosome carries the factor for long wings (Fig. 4, *A*), the result will be to produce a fertilized egg (Fig. 4, *C*) in which one member of the pair of chromosomes in question comes from the mother and carries the factor for long, and the other comes from the father and carries the factor for vestigial wing. Since this egg with both factors present produces a fly with long wings, the vestigial character is said to be recessive to the long; or conversely the long is said to be dominant to the vestigial character.

When the eggs and the sperm of hybrid flies of this origin come to maturity, the homologous chromo-

somes conjugate in pairs, as shown diagrammatically in Fig. 5, *b*. The chromosomes then separate (Fig. 5, *c* and *d*) at the time of division of the cell, and one of the resulting daughter cells gets the chromosome bearing the vestigial, and the other daughter cell gets the homologous chromosome, bearing the long factor. Hence, there will be two kinds of eggs in the female and two kinds of spermatozoa in the male. When two such hybrid flies mate with each other, any

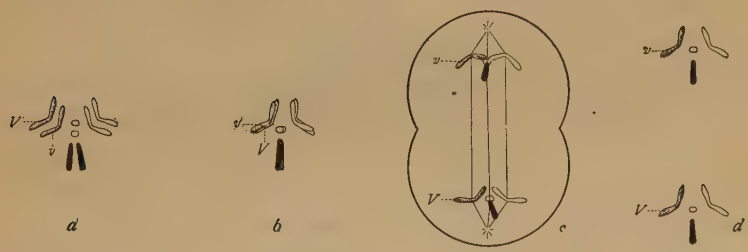


FIG. 5.—Diagram to illustrate in a heterozygous individual the conjugation and segregation of the chromosomes during "reduction."

sperm may meet and fertilize any egg. The possible combinations that result, and the frequency with which they occur, are shown in the next diagram (Fig. 6, and also in Fig. 3.)

As shown in this diagram, a sperm bearing the factor for long fertilizing an egg bearing the same factor produces a fly pure (homozygous) for long wings; a sperm bearing the factor for long fertilizing an egg bearing the factor for vestigial wings produces a hybrid fly (heterozygous) that has long wings, since, as above, the long "dominates" the vestigial character.

Similarly, a sperm bearing the factor for vestigial fertilizing an egg bearing the factor for long produces a hybrid, or heterozygote, with long wings; a sperm bearing the factor for vestigial fertilizing an egg

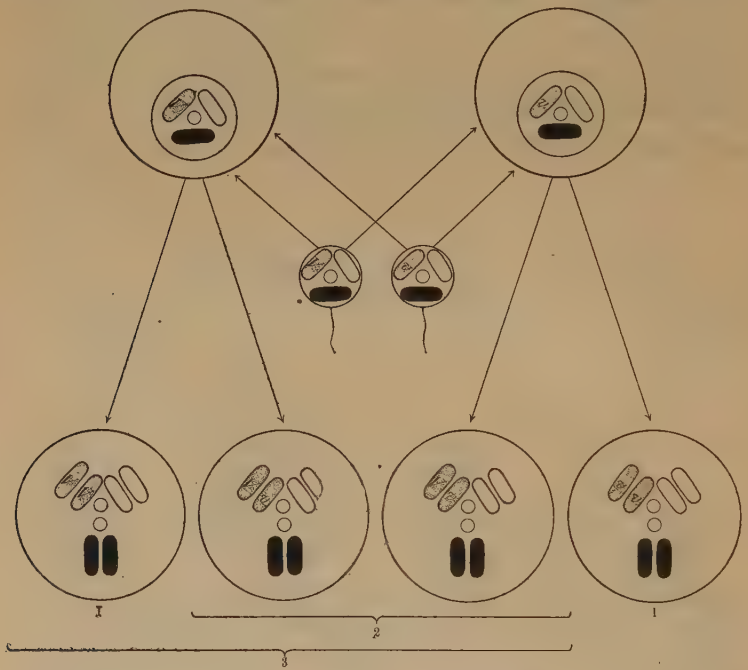


FIG. 6.—Diagram to illustrate how by the random meeting of two kinds of sperm and two kinds of eggs the typical 3:1 ratio results.

bearing the same factor produces a homozygote, having the recessive character vestigial wings.

Since the sperm and the eggs meet at random there should be 1 long VV, to 2 long Vv, to 1 vestigial vv; or, putting together all flies with long wings, 3 long to 1 vestigial. Three to one is the character-

istic Mendelian ratio when one pair of characters is involved.

In a third-chromosome stock, ebony, the body and wings are very dark in contrast to the wild fly whose color is "gray." Gray is used to designate the color of the wild fly, whose wings are gray, but whose body is yellowish with black bands on the abdomen. If ebony is crossed to gray the offspring (F_1) are gray but are somewhat darker than the ordinary wild flies. When these hybrids are inbred they give (F_2) 1 gray, to 2 intermediates, to 1 ebony. The group of intermediates in the second generation (F_2) can not be separated accurately from the pure gray type. If they are counted as gray, the result is three grays to one ebony.

Since ebony and gray assort independently of long and vestigial, as will be shown later, the factor for ebony must be supposed to be carried by a chromosome of a different pair from the one that carries vestigial. Since this chromosome behaves in the same way as does the one that bears the vestigial factor, the scheme used for vestigial will apply here also.

Another mutant stock is characterized by small eyes, and since in the extreme form it may lack one or both eyes entirely (Fig. 7), the name "eyeless" has been given to this mutant. When this stock is bred to wild flies the offspring have normal eyes. These inbred give three normal to one eyeless fly. As shown in the table on page 6, this character belongs in still another, the fourth, group, and its

mode of inheritance is explicable on the supposition that it lies in the fourth pair of chromosomes.

For an adequate understanding of the inheritance

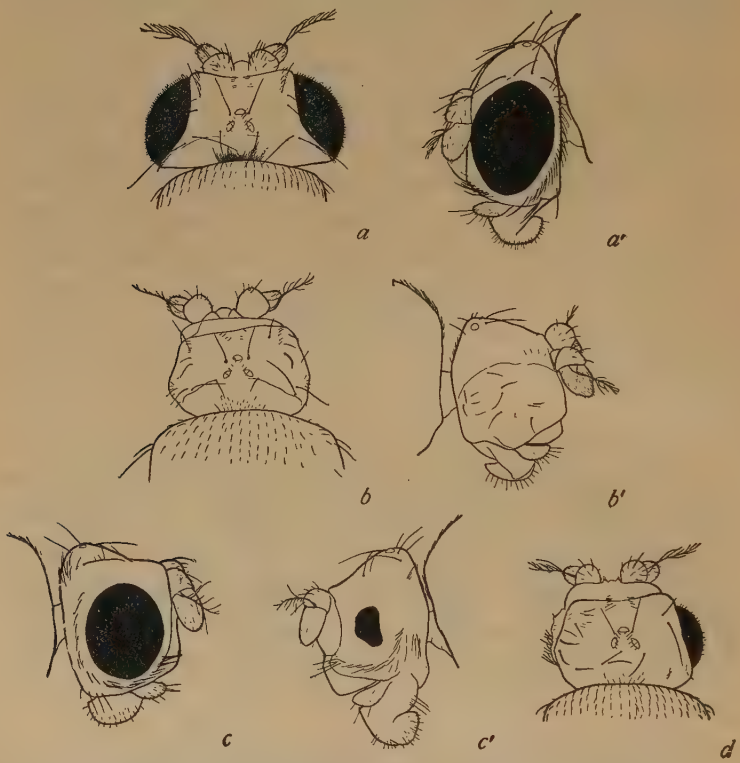


FIG. 7.—Normal eyes of Drosophila *a*, *a'*. Eyeless *b–d*; *b*, *b'* top and side view of head of fly without eyes; *c*, *c'* right and left eyes of another fly; *d*, small eye on right side, none on left.

of factors in the first group it will be necessary to consider the distribution of the sex chromosomes (Fig. 8). In the female of Drosophila there are two X chromosomes (XX). After the conjugation and

separation of the X chromosomes in the female there is one X chromosome left in each egg. In the male there is one X chromosome and another chromosome, its mate, called the Y chromosome. Hence in the male there are two classes of spermatozoa: one containing X, the other Y. If a Y-bearing spermatozoon should

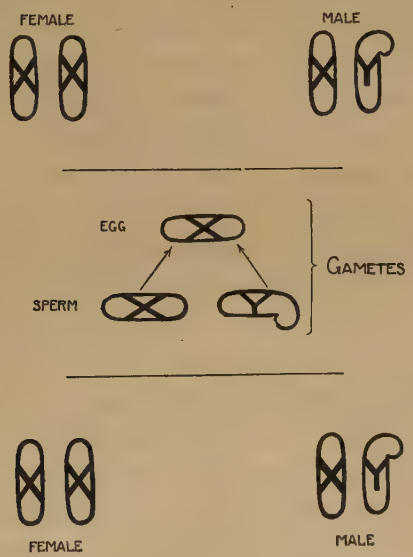


FIG. 8.—Diagram to show the history of the sex chromosomes from one generation to the next.

fertilize an egg the result will be an XY individual, or male. It is evident that the Y chromosome is found only in the males, while an X chromosome passes not only from female to female, but also from female to male and from male to female.

As will be shown now, certain factors follow the distribution of the X chromosomes and are there-

fore supposed to be contained in them. These factors are said to be sex linked.

The inheritance of white eyes may serve as an illustration for the entire group of sex linked characters. If a white-eyed male is bred to a red-eyed female (wild type) (Fig. 9), the sons and daughters (F_1) have red eyes. If these are inbred the offspring (F_2) are three reds to one white, but the white-eyed flies are all males. If we trace the history of the sex chromosomes we can see how this happens.

In the red-eyed mother, each egg contains an X chromosome bearing a factor for red eyes. In the white-eyed father, half of the spermatozoa contain an X chromosome which carries a factor for white eyes, while the other half contain a Y chromosome which carries no factors (Fig. 9). Any egg fertilized by an X-bearing spermatozoon of the white-eyed father will produce a female that has one red-producing X chromosome and one white-producing X chromosome (Fig. 9). Her eyes are red, because red dominates white. Any egg fertilized by a Y-bearing spermatozoon of the white-eyed father will produce a son (Fig. 9) that has red eyes, because his X chromosome brings in the red factor from the mother, while the Y chromosome does not bring in any dominant factor. At the ripening of the germ cells in the F_1 female the number of chromosomes is reduced to half. There result two kinds of eggs, half with the red-bearing and half with the white-bearing X (Fig. 9). Similarly in the male there will be two classes of sperm, half with the red-bearing X chromosome,

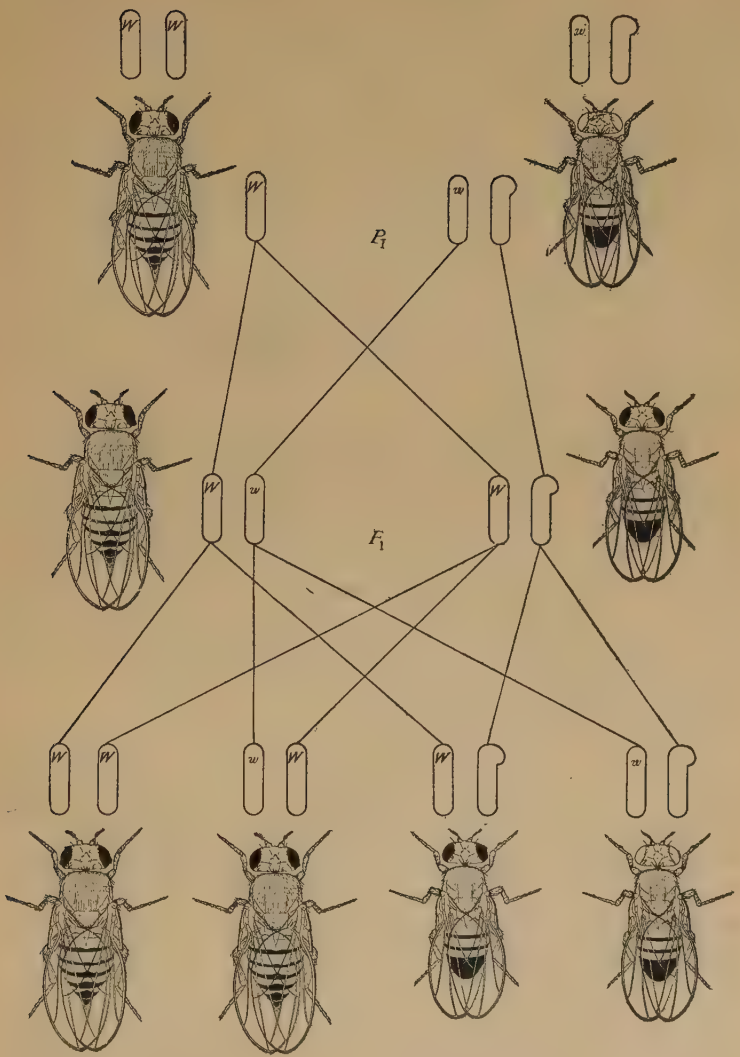


FIG. 9.—Red-eyed female by white-eyed male (D. melanogaster). This is the reciprocal of the cross shown in Fig. 10.

half with the indifferent Y chromosome. Random meeting of eggs and sperm will give the result shown in the lower line of the diagram. There will be a 3 : 1 ratio, as in other Mendelian crosses, but the white individuals in F_2 will be males. The factor for red in the F_1 male will always stay in the X chromosome, so that all the female-producing spermatozoa will carry red, and consequently all F_2 females will be red. The males will have red eyes if they receive the red-bearing chromosome from their mother and white eyes if they receive the white-bearing chromosome from their mother.

The reciprocal cross is made by mating a white-eyed female to a red-eyed male (Fig. 10). The daughters will have red eyes and the sons white eyes. If these are inbred their offspring will be red and white in equal numbers, and not the usual three reds to one white. The explanation of this new ratio is at once apparent as soon as the history of the sex chromosomes is studied.

The two X chromosomes in the white-eyed mother carry the factor for white eyes. After ripening, each egg carries one white-bearing X chromosome. The single X chromosome of the female-producing spermatozoon of the red-eyed father carries the factor for red eyes; the male-producing spermatozoa carry the Y chromosome which, as stated above, is indifferent. Any egg fertilized by a spermatozoon containing the red-bearing X chromosome will produce a red daughter, because red dominates white. Conversely, any egg fertilized by the Y-bearing male-producing sper-

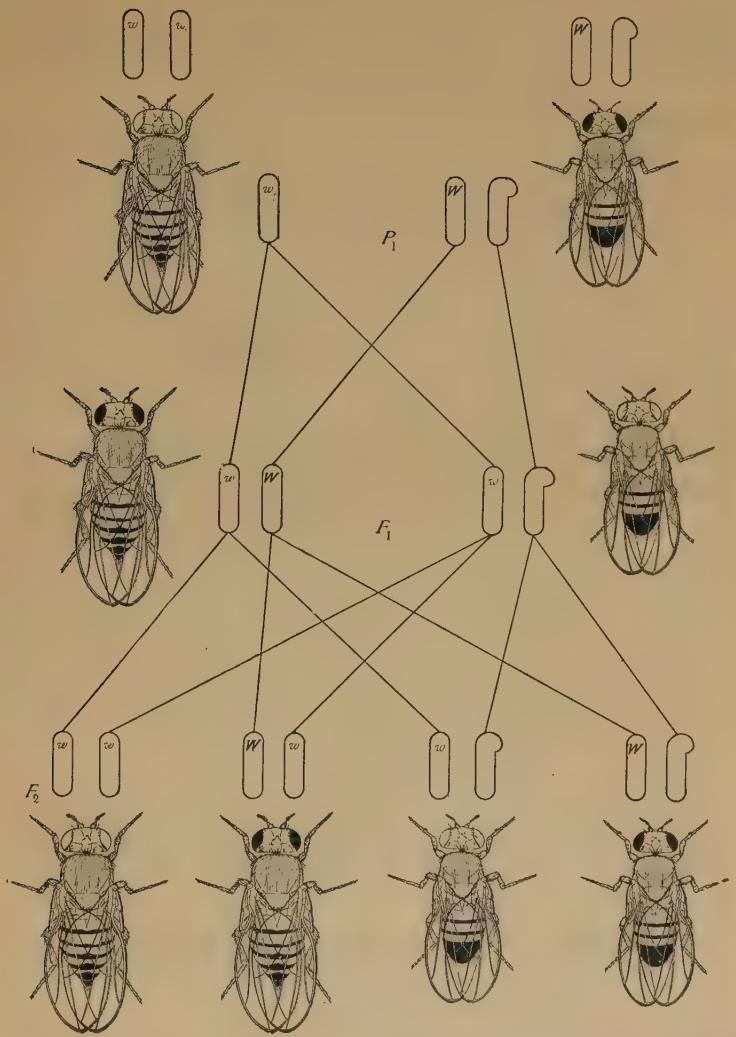


FIG. 10.—White-eyed female by red-eyed male (D. melanogaster). The factors for these characters are carried by the X chromosomes. In this diagram red is indicated by the symbol W and white by the symbol w. The history of the chromosomes is shown in the middle of the diagram.

matozoon will produce a white-eyed son, because the only X chromosome that the son contains is derived from his mother, both of whose X chromosomes carry a white-producing factor.

When these red-eyed daughters and white-eyed sons are inbred the possible combinations are shown in the lower line of the diagram (Fig. 10).

There will be two kinds of eggs, one containing a red-bearing, the other a white-bearing, X chromosome. The female-producing spermatozoa will contain a white-bearing X chromosome; the male-producing spermatozoa will contain a Y chromosome. A red-bearing egg fertilized by a female-producing spermatozoon will produce a red-eyed female; a white-bearing egg fertilized by a female-producing spermatozoon will produce a white-eyed female. A red-bearing egg fertilized by a male-producing spermatozoon will produce a red-eyed male; a white-bearing egg fertilized by a male-producing spermatozoon will produce a white-eyed male. The resulting ratio is 1 red to 1 white, in both sexes.

The distribution of the chromosomes explains how in one cross the Mendelian ratio of 3 :1 obtains, and also how in the reciprocal cross there is a 1:1 ratio.

The Inheritance of Two or More Independent Pairs of Factors

The application of the chromosome hypothesis to crosses between races that differ in two pairs of factors is illustrated by the following example (Fig.

11). If a vestigial gray fly is mated to a long-winged ebony fly, all the offspring (F_1) will have long wings and gray (or slightly darker) body color. If these hybrids (F_1) are inbred, offspring (F_2) will be produced in the ratios:

9 Flies with *long* wings and *gray* body color.
3 Flies with *vestigial* wings and *gray* body color.
3 Flies with *long* wings and *ebony* body color.
1 Fly with *vestigial* wings and *ebony* body color.

In the diagram (Fig. 11) the two pairs of chromosomes that carry the genetic factors in question are represented by short rods. In the vestigial fly recessive factors for vestigial (v) are in the "second" chromosome. This same fly has two "third" chromosomes that carry only normal factors, hence a pair of factors normal for ebony (E). In the ebony fly the third chromosomes carry recessive factors for ebony (e), while the second chromosomes carry the normal factors for vestigial (V). The formulæ for the two parents are vvEE and VVee, and their germ cells, respectively, vE and Ve.

The F_1 fly will have the composition vVEe, and will show neither the vestigial nor the ebony character. It is heterozygous in each pair of factors—*i.e.* one member of the second pair of chromosomes carries v, the other V; similarly, for the third pair of chromosomes, one member carries the factor e and the other the normal allelomorph E.

In the maturation of the germ cells of the hybrid, the members of each pair separate from each other as shown in Fig. 11 in the gametogenesis of F_1.

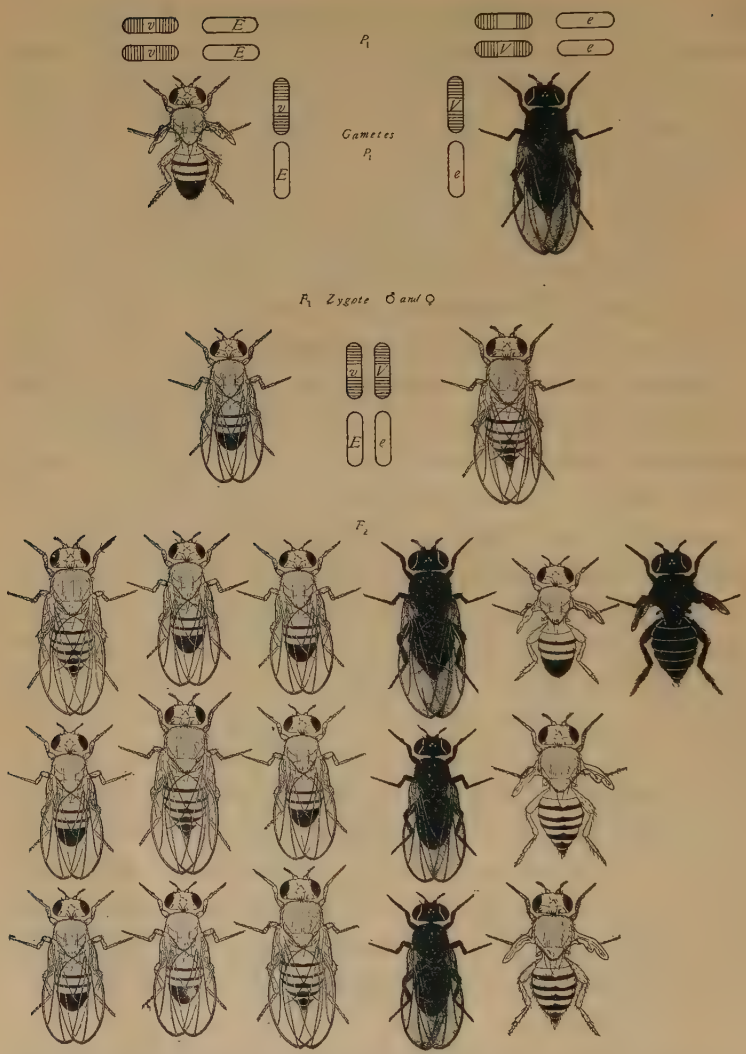


FIG. 11.—Diagram illustrating assortment of two mutant characters, vestigial and ebony.

The two pairs of chromosomes "assort" on the spindle in either one of the two ways shown in the diagram; resulting in four and only four kinds of gametes.

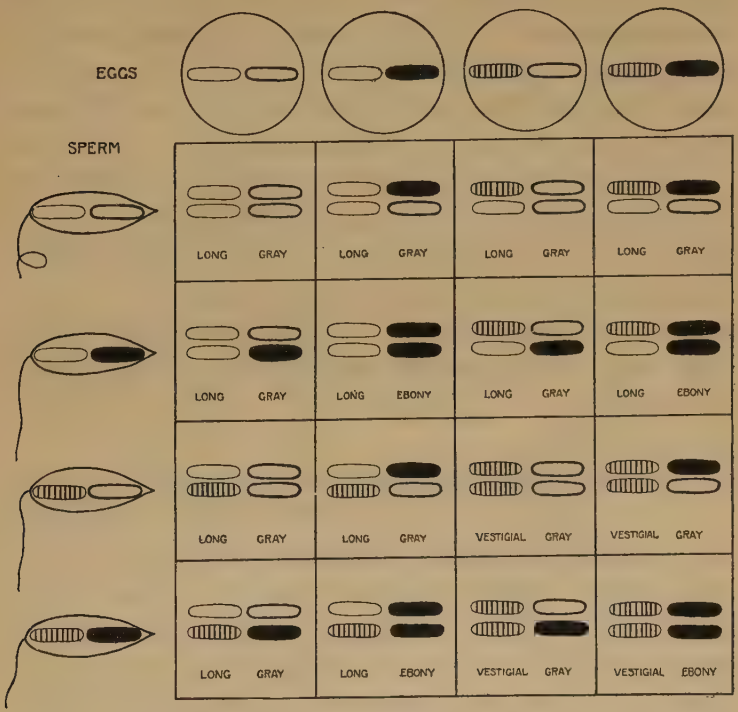


FIG. 12.—Diagram to show the 16 possible kinds of permutations of the four kinds of gametes of Fig. 11. Along the top line are four kinds of eggs; along the left side are four kinds of sperm; in the squares are the combinations formed by the meeting of each kind of egg with each kind of sperm, giving 9 long gray; 3 long ebony; 3 vestigial gray; 1 vestigial ebony.

The process just described takes place both in the male and in the female. Consequently there will be four kinds of eggs and four kinds of spermatozoa.

Chance meeting between these will give the results shown in the next diagram (Fig. 12).

In the table (Fig. 12) the four kinds of eggs are represented at the head of the four vertical columns, and the four kinds of spermatozoa at the left of each horizontal row. In the squares the combination of each kind of sperm with each kind of egg is represented, giving the ratio of 9 long gray: 3 vestigial gray: 3 long ebony: 1 vestigial ebony.

The F_2 expectation may, of course, be derived more directly as follows: There will be 3 long to 1 vestigial. These longs will be both gray and ebony in the ratio again of 3 to 1; hence 9 long gray to 3 long ebony. Correspondingly, the vestigials will be both gray and ebony, in the ratio of 3 to 1; hence 3 vestigial gray to 1 vestigial ebony. The result is the same as before.

If one of two independent pairs of characters is sex linked, the same scheme holds in those cases where the recessive sex linked character enters through the grandfather, but the ratio is different when the recessive sex linked character enters through the grandmother (viz., 3 :3 :1 :1), as is to be expected from the mode of inheritance of white eyes taken alone;[1] and here, too, the result conforms fully to the chromosome scheme.

Three factors can be worked out by means of the

[1] For example, taking white and red alone the ratio of the F_2 is 1 :1. But among the reds the ratio of gray to ebony will be 3 :1 and among the whites will be 3 :1. Hence the result 3 red gray, 1 red ebony, 3 white gray, 1 white ebony.

chromosomes as readily as one or two. It will not be necessary to give the full analysis, for it will be easily understood from the scheme already given. If a fly with vestigial wings is crossed to an ebony, eyeless fly three pairs of factors are involved that lie in different chromosomes. The F_1 flies are normal, for there is in the hybrid a normal mate for each of the three recessive factors. The possible recombinations are shown in the next diagram, Fig. 13. There

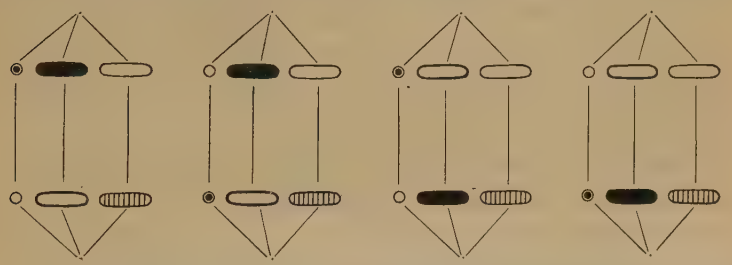


FIG. 13.—Diagram to show the segregation of the three pairs of chromosomes. Eight combinations are possible, giving 8 kinds of germ cells, with 64 possible re-combinations.

are four different positions for the chromosome pairs on the spindle, leading to eight kinds of germ cells. By chance meetings of the eight kinds of sperm with the eight kinds of eggs there will result 8 types as follows:

27 Long, gray, normal eye (wild type).
9 *Vestigial*, gray, normal eye.
9 Long, *ebony*, normal eye.
9 Long, gray, *eyeless*.
3 *Vestigial*, *ebony*, normal eye.
3 *Vestigial*, gray, *eyeless*.
3 Long, *ebony*, *eyeless*.
1 *Vestigial*, *ebony*, *eyeless*.

The same manner of treatment will work for more than three pairs of chromosomes; the number of kinds of germ cells increases in geometrical ratio. In most animals and plants the number of chromosomes is higher than in Drosophila, and the number of pairs of factors that may show independent assortment is, in consequence, increased. In the snail, Helix hortensis, the half number of the chromosomes is given as 22; in the potato beetle 18; in man, probably, 24; in the mouse 20; in cotton 28; in the four-o'clock 16; in the garden pea 7; in corn 10; in the evening primrose 7; in the nightshade 36; in tobacco 24; in the tomato 12; in wheat 8. If 20 pairs of chromosomes are present there will be over one million possible kinds of germ cells in the F_1 hybrid. The number of combinations that two such sets of germ cells may produce through fertilization is enormously greater. From this point of view we can understand the absence of identical individuals in such mixed types as the human race. The chance of identity is still further decreased since in addition there may be very large numbers of factors within each chromosome.

CHAPTER II

TYPES OF MENDELIAN HEREDITY

Experience has shown that Mendelian inheritance applies to all sorts of characters, structural, physiological, pathological, and psychological; to characters peculiar to the egg, to the young, and even to old age; to length of life; to fundamental taxonomic characters as well as to "superficial" characters; and to characters intimately concerned in maintaining the life of the individual, as well as to characters which apparently do not influence survival. Some of these different types and their mode of inheritance will be briefly described, but since the general principles involved are more important than the kind of character that is affected, the results will be treated under general headings.

Dominance and Recessiveness

The four-o'clock (Mirabilis jalapa) has a white and a red-flowered variety. If these are crossed the hybrid is pink in color. The pink hybrid inbred (self-fertilized in this case) gives in the next generation (F_2) one red, to two pink, to one white (Fig. 14). Owing to the intermediate color of the hybrid (or heterozygote) it is impossible to say that either color dominates the other. The factor for red and

the factor for white both affect the plant in which they occur. In this and in similar cases the F_2 ratio of 1 : 2 : 1 is obtained, because it is possible to distinguish the pure red and the pure white from the heterozygous plants.

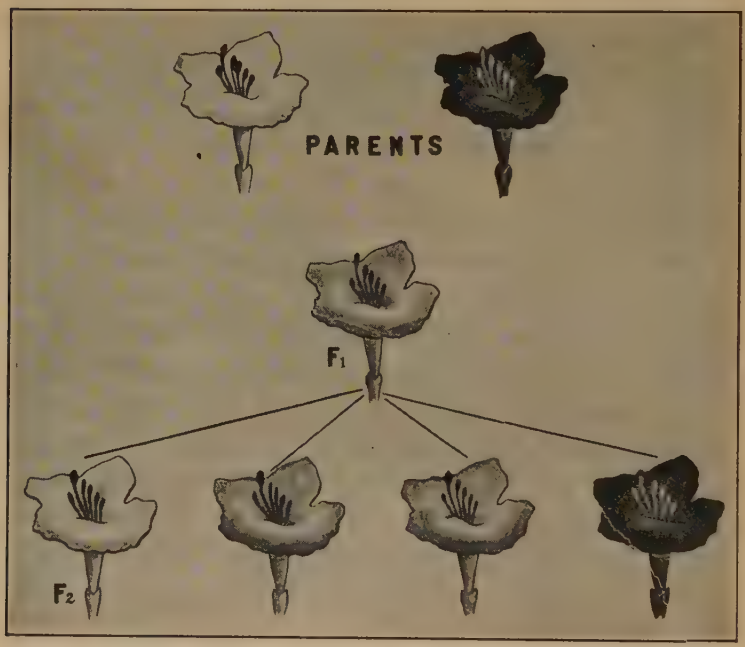


FIG. 14.—Diagram to illustrate the cross between a red and a white flowered Mirabilis jalapa (4 o'clock), which produces a pink, intermediate heterozygote.

The Andalusian fowl is a similar case. When certain races of black are bred to certain races or kinds of "white" the hybrid is slate "blue" in color. These blue birds, called Andalusians, when inbred, give one black to two blue to one white. Blue is

the heterozygous condition; it is not possible to produce a pure breeding race of Andalusians, for the combination that produced an Andalusian falls apart in the germ cells of the Andalusian birds. The bird is blue because the pigment is not spread evenly over the feather but is restricted to small but black specks.

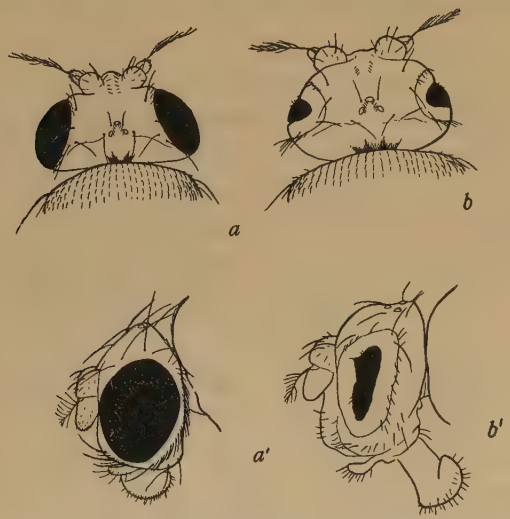


FIG. 15.—Normal (*a*, *a'*) and bar eye (*b*, *b'*) of Drosophila; shown in side view, and as seen from above.

The Andalusian blue is a mosaic of black and white, and not at all a dilute black.

A good example of an intermediate hybrid is found when the mutant fly with bar eye (Fig. 15) is bred to a wild fly. The daughters have bar eyes that are not as narrow as those of the pure bar stock. The range of variation is great, however, for some of the hybrids have eyes that are nearly as round as the normal, and

in others the eye is nearly as narrow a bar as that of pure stock. In the male, which has one factor for bar eye, the eye is as narrow as in the pure (*i.e.*, homozygous) female with two factors. The intermediate condition in the female which is hybrid (heterozygous) for this factor is hence not explained by the lesser effect of the single factor, but is probably due to the competing influence of the other allelomorph. Of course it might be contended that since in the male there is a different chromosome complex (XABCD YABCD) from that in the female (XABCD-XABCD) it is this difference in other factors that causes the heterozygous female to have a wider eye than the male; but this argument is rendered improbable here, when we recall that in only one out of many cases of sex linked inheritance, in which the heterozygous female is intermediate, is the male different from the homozygous female.

In other cases the influence of one of the parents of the cross may be so slight as to escape detection on ordinary observation, and may require special measurements for demonstration. When flies with miniature wings (Fig. 16) are mated to wild flies, the daughters have long wings, which Lutz has shown to be a little shorter in proportion to the length of the legs than are the wings of wild females; but the difference is so slight that it could not have been detected without biometrical methods.

Finally, we must consider the class of cases in which complete dominance has been described. All the cases given by Mendel in peas were supposed

to fall under this heading: yellow dominates green, round dominates wrinkled, etc.

Whether a character is completely dominant or not appears to be a matter of no special significance. In fact the failure of many characters to show complete dominance raises a doubt as to whether there is such

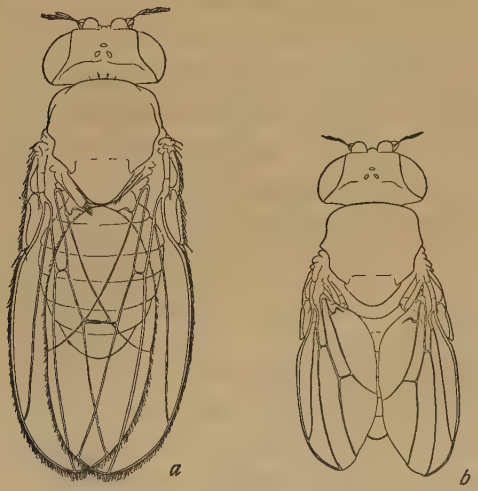


FIG. 16.—*a*, Long wing (wild type) of Drosophila; *b*, miniature wing. (*a* and *b* are not drawn to scale.)

a condition as complete dominance. Some cases approach so nearly to that condition that special tests may be required to show that the hybrid is affected by the recessive factor. For instance, in flies the factor for white eyes seems to produce no effect when white is bred to red. The F_1 reds are indistinguishable from pure reds. But by weakening the red by adding recessive factors other than white, the influence of white can be demonstrated, as Mor-

gan and Bridges have shown. Therefore although the effect of the white factor can not be detected in the single combination with red, it is reasonable to suppose that some effect is really present. Similarly, conditions were found in which the effect of heterozygosis for eosin, vermilion, or pink could be demonstrated. While the question is one of only subsidiary importance, yet in the separation of classes it is often useful to be able to distinguish the pure from the hybrid form; but whether this can or can not be done in any given case does not affect the fundamental principle of segregation which is the essential feature of Mendel's discovery.

Manifold Effects of Single Factors

It is customary to speak of a particular character as the product of a single factor, as though the factor affected only a particular color, or structure, or part of the organism. But everyone familiar at first hand with Mendelian inheritance knows that the so-called unit character is only the most obvious or most significant product of the postulated factor. Most students of Mendelian heredity will freely grant that the effects of a factor may be far-reaching and manifold. A few examples may make this plain.

In Drosophila there is a mutant stock called "club," in which the wing pads fail to unfold (Fig. 17) in about 20 per cent. of the flies. In the majority of club flies the wings expand fully, and are like those of the wild fly. Owing to this fact, that not all the

flies even in a pure stock of club show this character, it was difficult to study the inheritance of the supposed factor that sometimes inhibits the unfolding of the wing pads. Nevertheless, it was possible even with this handicap to show that the character depended on a sex linked recessive factor. Later

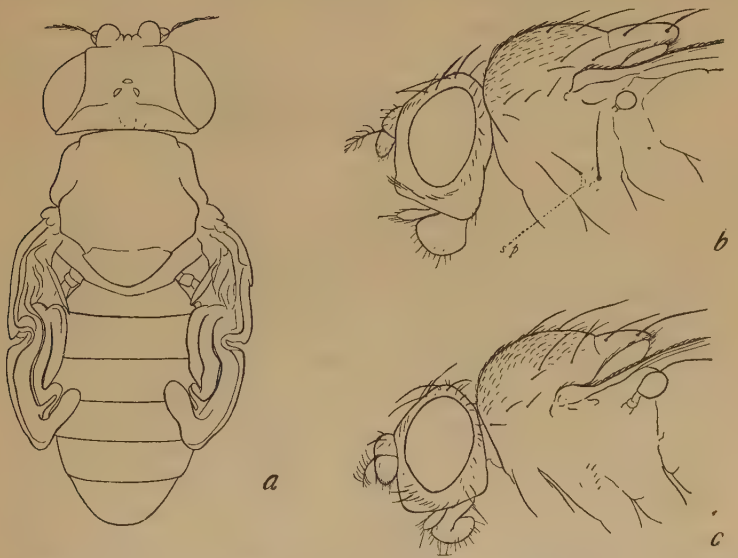


FIG. 17.—Club wing (to left). The absence of the spines on the side of the thorax in "club" is shown in *c*, and the normal condition is shown in *b*.

the discovery was made that a particular pair of spines always present on the side of the thorax of the wild flies, is absent from the club flies, irrespective of whether the wings do or do not unfold (Fig. 17, *c*). This constant feature of the mutant made its study quite simple. Another pair of spines, those upon the

rear margin of the scutellum, point constantly in an abnormal direction in club stock. The head of club flies is often flattened, the eyes are smaller, and the thorax and abdomen are somewhat distorted. Here we have an example of a single germinal difference, the factor for club, producing several distinct effects,

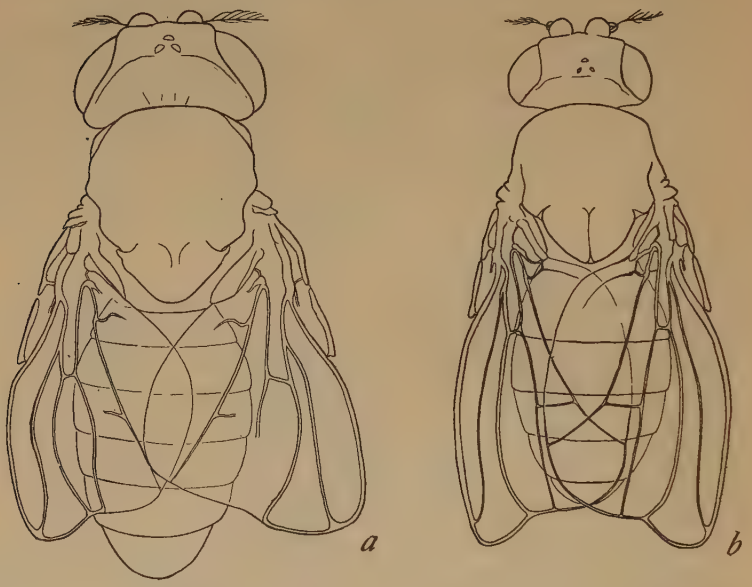


FIG. 18.—Rudimentary wing (to left), and truncate wing (to right).

some of which are constant features of the stock, while others are occasional or variable.

Another and similar example is found in the rudimentary winged flies (Fig. 18, *a*). The wing is usually shorter than the abdomen, but may be longer and even approach the normal wing in length and shape. The

last pair of legs are often thicker and shorter. If many larvæ are present, or the food conditions poor, the larvæ of rudimentary flies can not stand the competition and die off, and in consequence the rudimentary class is smaller than expected. The males are fertile, but the females are almost entirely sterile, although rarely one of them may lay a few eggs and some of these hatch. The infertility is probably due to absence or rareness of mature eggs in the ovaries. There are also other effects than these four mentioned, all of which are produced by the same factor, and, no doubt, were our knowledge complete, we should find in all mutants many differences in addition to the ones picked out for study and called "unit characters." DeVries' definition of mutation entirely covers this relation; in fact, it even goes further and implies that a single difference may affect the entire organization. Perhaps this does occur, but practically the number of differences that can be *observed* between a wild and a mutant stock derived from it, is limited. The attack that is sometimes made on the unit character hypothesis fails in its intention the moment it is understood that a single factor (difference) has generally not one but many effects. Most workers in Mendelian heredity are fully conversant with these facts. This attack on the unit character conception is usually made by those not familiar with the actual situation and who take the expression unit character too literally. It may be conceded that the expression has at times been abused even by some of Mendel's followers.

Similar Effects Produced by Different Factors

There are many cases in which characters that are superficially alike are the product of different factors. White color that characterizes so many domesticated races of plants and animals is a case in point. There are two pure breeding races of white flowered sweet peas. When crossed, they produce colored flowers. When the F_1 offspring are inbred the F_2 generation consists of 9 reds to 7 whites. This 9 : 7 ratio is a special case of the 9 : 3 : 3 : 1, in which the last three classes are superficially alike. The explanation here is that there are two kinds of recessive whites that have originated independently. On the chromosome hypothesis one white is due to mutation in one chromosome and the other white to mutation in another chromosome. When the races are crossed, each race supplies that chromosome which contains the normal factor of the white of the other race. In the F_2 generation any plant that contains at least one of the normal chromosomes of both pairs will not be white. There will be nine such cases. Any plant that contains both of the white-producing chromosomes of either pair will be white. There will be seven such cases.

There are also two pure races of white fowls that, when crossed, give colored birds. Each white behaves as a recessive to color. For instance, the white silky crossed to a white dorking gives colored birds. These inbred give 9 colored to 7 white birds.

There is a third kind of white race of poultry, namely, white Leghorn, in which white is dominant. Crossed to colored birds the offspring are white (with often a few colored feathers, which indicates that dominance is not complete).

In the silkworm also a dominant white and a recessive white factor have been found. The genetic results are comparable in all respects to those in the fowl.

There are also cases of blacks or melanic types, that have different factorial bases. There are three black races of Drosophila—called sable, black, and ebony—that belong respectively to the first, second, and third groups. These are much alike, but close scrutiny reveals slight differences. Any two crossed together give gray F_1 flies.

There are three pink eye colors in Drosophila, one whose locus is in the third chromosome (pink), and two sex linked eye colors which are so similar that no certain difference between them can be observed.

Not only pigment but also structural characters may parallel each other in a remarkable manner. For example, in Drosophila the mutant stocks "bow" (sex linked) and "arc" (II chromosome) have wings that curve evenly downward over the abdomen. There are also two kinds of flies whose wings turn up sharply near the ends. These stocks are "jaunty" (second chromosome) and "jaunty I," which is sex linked. Two types, called "fringed" (II chromosome) and "spread" (III chromosome), are characterized by thin textured wings held out nearly at right

angles to the body. In the case of rudimentary and truncate (Fig. 18) the wings are so similar that without breeding tests one of them might easily be taken for the other. Finally, "facet" and "rough" both have the ommatidia of the eye disarranged very much in the same way.

Modification of the Effects of Factors

I. By Environmental Influences

It is a commonplace that the environment is essential for the development of any trait, and that traits may differ according to the environment in which they develop. In most cases different genetic types produce different results in any ordinary environment. The environment, being common to the two, may therefore in such cases be ignored, or rather taken for granted. There are other cases, however, in which a particular genetic type appears different from another one only in a special environment. Where this environment is not the normal one, its discovery is an essential element of the experiment.

One of the best cases is that given by Baur. The red primrose (Primula sinensis rubra) reared at a temperature of 30°–35° C. (with moisture and shade) has pure white flowers, but the same plants reared at 15°–20° have red flowers. If the white-bearing plants are brought into a cooler place, the flowers that are already in bloom remain white, but those that develop later in the cooler temperature are red. There

is another race of primula (Primula sinensis alba) that always has white flowers, even at 20°. Strictly speaking, we should say, not as we generally do for brevity's sake, that the difference between the two races is that one has white, the other red flowers, but we should say rather that P. rubra reacts at 20° by producing red, at 30° by forming white flowers; P. alba, on the other hand, reacts both at 20° and at 30° by producing white flowers. The constant difference between these races is not in their color, but in the possibility of producing specific colors at certain temperatures.

This is the point of view, of course, that must also be taken for cases in which differences exist in all the usual environments; for, here also, it is the different possibilities of reaction that are inherited. Brevity warrants us in speaking of particular characters as inherited, rather than the specific possibility of reaction that gave these characters; but no one need be misled by the shorter expression.

Two similar cases of the influence of the environment have been found in Drosophila. There is a mutant stock known as abnormal abdomen in which the normal black bands of the abdomen are broken and irregular or even entirely absent (Fig. 19). In flies reared on moist food the abnormality is extreme; but even in the same culture the flies that continue to hatch become less and less abnormal as the culture becomes more dry and the food scarce, until finally the flies that emerge later can not be told from normal flies. If the culture is kept well fed the change does

not occur, but if the flies are reared on dry food they are normal from the beginning. The character is a sex linked dominant, as shown by the following crosses. When an abnormal male is bred to a normal (wild) female, the daughters are abnormal (if the

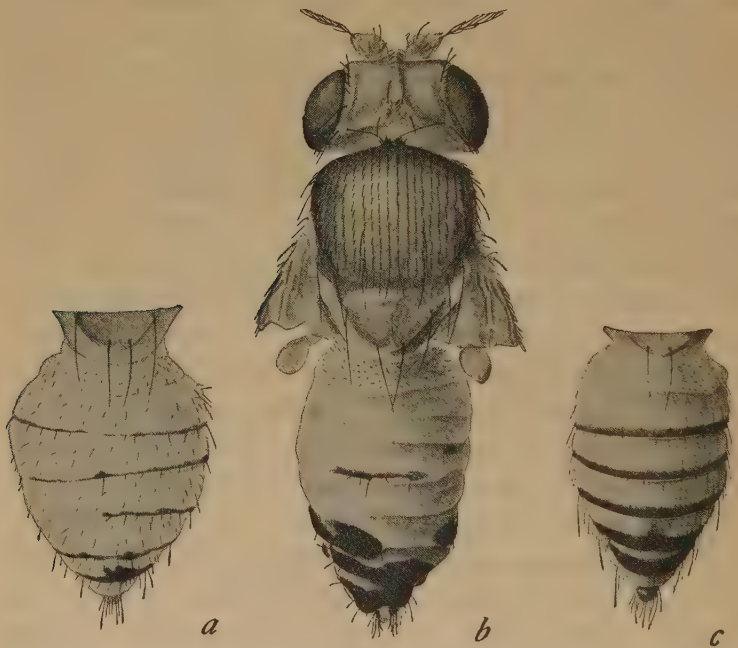


FIG. 19.—Mutant type called Abnormal Abdomen of Drosophila ampelophila (the wings have been cut off); *a* is female; *b*, male; *c*, female that approaches the normal type.

food is moist), but all the sons are normal. If the medium is dry, however, both the daughters and the sons alike are normal. But these normal F_1 daughters will produce the expected abnormal offspring if the conditions are suitable, and these offspring are just as

abnormal as though the female had herself been abnormal. The reciprocal cross, viz., abnormal females by normal males, gives abnormal sons and daughters, if the food is suitable, but normal if the food is dry, etc. In both cases the F_2 gives the expectation for a sex-linked dominant factor if the medium is suited to bring out the abnormal character, and the result is entirely obscured if the food is dry. Here, at will, we can demonstrate a regular Mendelian ratio by control of the environment, and conversely, we can conceal completely what is taking place by substituting another environment. That the same genetic process is going on in both cases can be demonstrated by suitable tests.

A case similar in principle occurs in a mutant stock of Drosophila that produces supernumerary legs. This stock was observed in winter to produce a considerable percentage of flies with supernumerary legs, but few or none in summer, especially in warm weather. Miss Hoge, who has studied this stock, finds that when the flies are kept in an ice chest at a temperature about 10° C. a high percentage of flies with supernumerary legs occurs. Sometimes several legs or parts of a leg are doubled, or the doubling may occur twice in the same leg. The general rule that Bateson pointed out for duplicated legs in other insects appears to hold here, viz., the adjacent parts are mirror images of each other.

In the cold the duplicate leg gives a regular Mendelian result; but at normal temperature the duplication is a rare event and its mode of inheritance

obscured. In a hot climate there would be no evidence that such a factor was being regularly transmitted. But if the type moved into a cold region it would show duplication in many of the legs.

II. By Developmental Influences

"Age," too, is in a sense an environmental condition, which influences the development of characters. Thus a white flower may change to purple as the plant gets older, or the flaxen hair of a child may turn to brown when he becomes a man. But, as in the case of other "environmental" conditions, age may not have the same effect on individuals with different factors; in this way it comes about that animals or plants which differ by certain factors may show a difference in character only at certain ages, or may not show the same difference at all ages. In Drosophila, flies with the factor for pink eyes are easily distinguishable from those with the factor for purple eyes, when the flies are young, but as they grow older, the eyes of both races assume a dark purplish shade, and become practically indistinguishable from each other. Conversely, old flies with the factor for black are usually easy to separate from those having the normal "gray" factor, but the newly hatched flies, in which the black pigment is not yet fully developed, are separated with greater difficulty.

These cases in which a factor-difference has a visible effect only at a certain age are in no fundamental respect different from cases like that of the Drosophila

with reduplicated legs, where a factor difference has a visible effect only under special external circumstances.

A number of cases of Mendelian inheritance are known in which only the larvæ, and not the adults, are affected. Tower has described crosses in which the beetle Leptinotarsa signaticollis was crossed with L. undecimlineata (Fig. 20, *A*, *B*). In the first stage (*C*), the larvæ of these two beetles are exactly alike, but in the second stage, the larvæ of L. undecimlineata are white and the larvæ of L. signaticollis are yellow; and in the third stage the undecimlineata larvæ are still white without stripes, while the others have well-developed tergal stripes (*B*). When these species are crossed under certain external conditions the F_1 larvæ are yellow and, later, striped. The beetles that come from them are intermediate. Inbred, these beetles give three larvæ of the yellow type to one of the white type.

There is extensive evidence from cytology, experimental embryology, and regeneration, to show that all the different cells of the body receive the same hereditary factors. We must suppose, then, that the Mendelian factors are not sorted out, each to its appropriate cell, so that factors for color go only to pigment cells, factors for wing-shape to cells of the wings, etc., but that differentiation is due to the cumulative effect of regional differences in the egg and embryo, reacting with a complex factorial background that is the same in every cell. These regional peculiarities of different parts of the egg and embryo, may,

like the age of the individual, also be considered as influences external to the hereditary factors which affect the development of characters. And not only

FIG. 20.—Leptinotarsa signaticollis (above), and L. undecimlineata (below), with their full grown (*B*) and second stage (*C*) larvæ to the right of each. (After Tower.)

do regional peculiarities influence characters, but special regions are usually required for a given factor difference to manifest itself, just as certain temperatures or ages may be necessary. Thus when we

speak of factors for eyes or for legs, we really mean factor-differences which can produce effects only in the eye, the leg, or other regions of the body. In other cases the expression of a factor-difference may not be limited to one region but may produce a different effect in different regions; for example, a gray white-bellied mouse, which differs from the yellow mouse by only a single factor, is lighter than yellow on the under side, but darker on the upper side.

III. By the Influence of Other Factors

Analogous also is the fact that certain factor-differences produce a visible effect only when they are in company with a particular complex of other hereditary factors. Thus, a fly with the factors for vermilion eyes can not be distinguished from one with the factors for pink eyes if both contain, in addition, the factors for white eyes, for the factors for white allow no other color to develop. Again, it is obvious that without the factors necessary for the development of a given character, no factors merely determining special modifications of that character can have any effect. In other cases, the effect of a given factor may not be entirely suppressed, but greatly changed, if certain other factors in the hereditary complex are changed. Thus, in flies which already have the factor for vermilion eyes, the factor for purple eyes produces an eye still lighter than vermilion, but in flies containing the normal allelomorph of the factor for vermilion, the factor for purple pro-

duces an eye decidedly darker than normal. Such cases of interaction of factors, in which the effect of one factor is altered by the action of another factor, are very numerous.

IV. Conclusion

It would have been indeed strange if Mendelian factor-differences had not been found that require special conditions—environmental, developmental, or factorial—in order to produce a given effect, or any effect at all. For Mendelian factors may cause or influence all sorts of characters—that is, any or all kinds of developmental or physiological reactions; and many of these reactions are known to be affected by age, temperature, region of the body, and so forth. The facts given above are in no possible sense subversive to Mendelian principles. On the contrary they illustrate to great advantage the previously given interpretation of all hereditary characters—namely, that every character is the realized result of the reaction of hereditary factors with each other and with their environment. Failure to understand this viewpoint has led to some futile criticism by the opponents of the modern Mendelian interpretation in terms of unit factors. This criticism is as pointless as it would be to criticize the atomic theory on the ground that oxygen does not, under all conditions, and in all its compounds, give rise to substances with the same properties.

The validity of the unit factor conception rests

upon the fact that whenever (as often happens) all other conditions, external and internal, that modify characters remain constant, clear-cut ratios are obtained which can be explained only as due to segregation, in definite ways, of particular hereditary factors that perpetuate themselves unchanged from generation to generation. The validity of the factorial hypothesis may also be proved under circumstances not so well controlled, however. In cases where, on the factorial hypothesis, a certain factor is expected to be present in an individual, then, even if the individual fails to develop the character commonly taken as indicative of the factor, the actual presence of the factor may be demonstrated by breeding tests. For if, in subsequent generations, circumstances—genetic or environmental—are provided, like those in which the character previously appeared, it will again show itself. Flies of the race with abnormal abdomen, if raised in a dry bottle, appear perfectly normal, but the presence within them of the factor for abnormal may be demonstrated by rearing their offspring in a wet bottle. Again, the factor for pink eyes may be carried by a race with white eyes, and although pink does not show in the white-eyed race, its presence there may then be demonstrated by crosses of these flies with flies that are not white. Cases like these could be multiplied over and over again.

CHAPTER III

LINKAGE

If two factors lie in the same member of a chromosome pair we should expect them always to be found together in successive generations of a cross unless an interchange can take place between such a chromosome and the homologous chromosome derived from the other parent.

Whenever the two factors remain together in the same chromosome there will be formed equal numbers of gametes containing the two factors and of gametes containing the normal allelomorphs of the two factors. But if pieces of homologous chromosomes are interchanged, then some of the gametes will contain one of the factors in question, and an equal number will contain the other factor. The process of interchange between chromosomes is called crossing over; the tendency of factors to stay together is called linkage.

An example may make clearer this process of crossing over. The factor for black body color and that for vestigial wings both lie in the second pair of chromosomes. If a black vestigial fly is crossed to a wild fly (gray, long wings) (Fig. 21) the offspring are gray with long wings. These F_1 flies have one chromosome containing both the factor for black and the factor for vestigial, and a homologous chromosome

with the normal allelomorphs of these factors. After maturation one or the other of these chromosomes

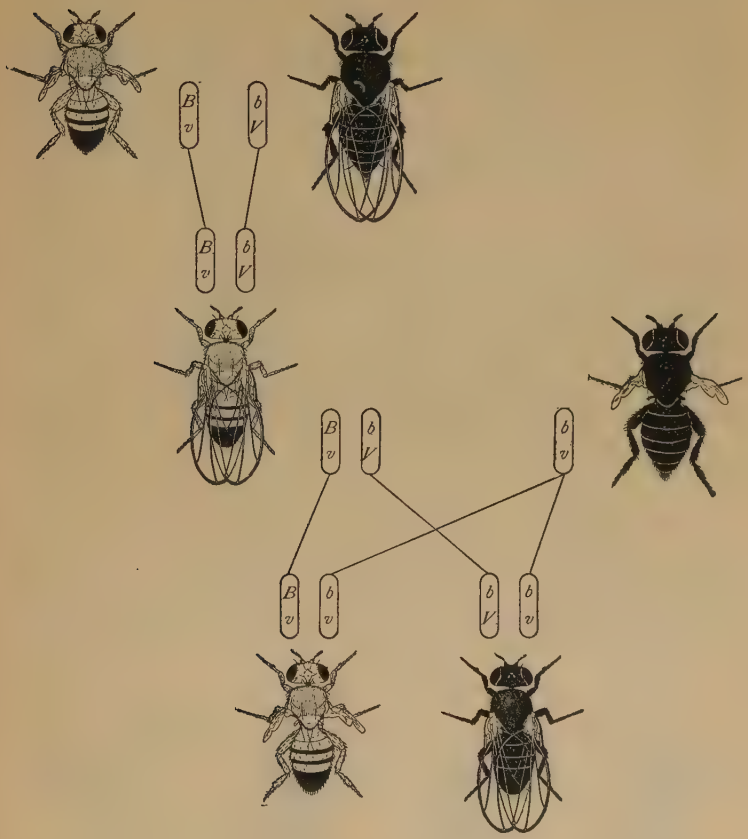


FIG. 21.—Back-cross of F_1 ♂ (out of vestigial by black) by black vestigial ♀.

will be left in each egg and each sperm. The gametes will consequently contain the same combinations of

factors as were present in P_1 unless an interchange has taken place between the two chromosomes. The best way to find out whether such an interchange has taken place is to mate the F_1 males and females to the double recessive type, black vestigial, because black and vestigial being recessive factors will not obscure the factors that are carried by the gametes of the F_1 to be tested. When the F_1 male is back-crossed to a black vestigial female, Fig. 21 (second line), only two classes of offspring are produced. Half of the flies are black vestigial and half are gray long. This must mean that there has been no crossing over in the hybrid F_1 male; for he produces only two kinds of gametes and these are of the kind that combined to produce him. In other words, the chromosomes received from his parents have remained intact.

If we test the F_1 female, by back-crossing to a black vestigial male, the result is different. If such a female is bred to the double recessive male, black vestigial, four kinds of offspring result, as follows:

Non-crossovers		Crossovers	
Black, vestigial	Gray, long	Black, long	Gray, vestigial
41.5 per cent.	41.5 per cent.	8.5 per cent.	8.5 per cent.
83 per cent.		17 per cent.	

Of these four classes the first two correspond to the combinations which the F_1 received from its parents, namely, black vestigial and gray long; the other two are classes that would be expected if crossing over had

taken place between black and vestigial in the pair of homologous chromosomes. The numerical results

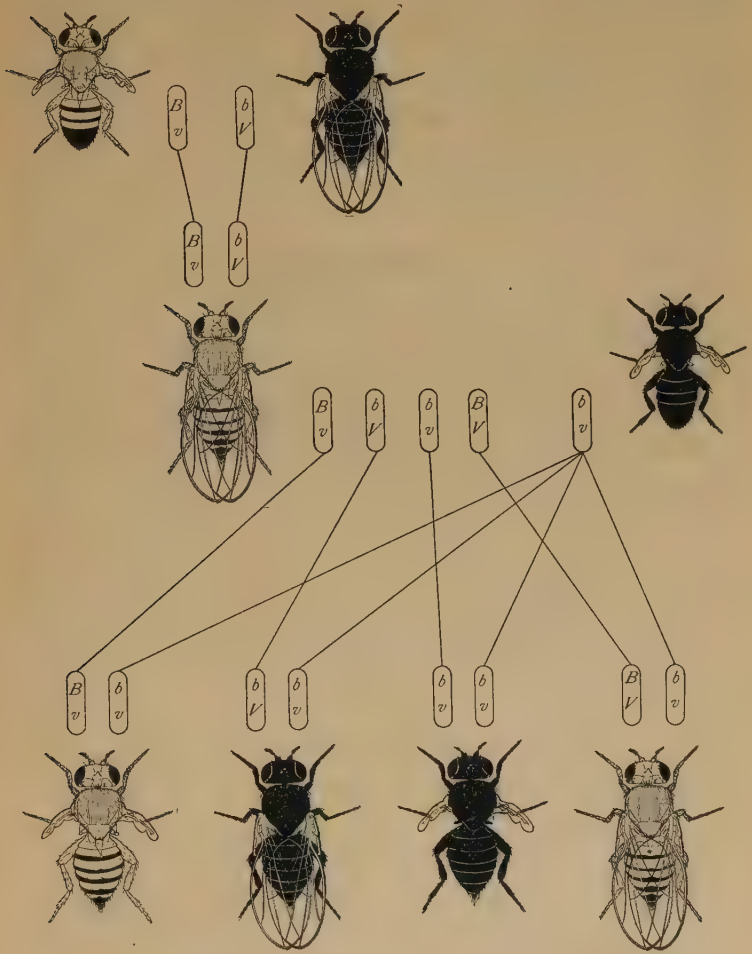


FIG. 22.—Back-cross of F_1 female (out of black by vestigial) by black vestigial male.

show that this crossing over takes place in about 17 per cent. of cases. In other words, the chances are

about five to one that the combination that went in holds together.

It is also instructive to repeat the cross in such a way that the two mutant factors, black and vestigial, enter from different sides, *i.e.*, one parent contributes black and the other vestigial. As shown in the next diagram (Fig. 22), each parent carries in its chromosome one mutant factor and the normal allelomorph of the other.

If the F_1 males are backcrossed to black vestigial females only two classes result, viz., black long and gray vestigial Fig. 22 (third line). These are the combinations that entered; hence no crossing over has taken place in the F_1 males. We see that here the linkage is not due to some affinity between the factors black and vestigial, *per se*, for in this cross they always enter different gametes as surely as they stayed together before. The reason for this difference in result is that in this cross they came from different parents and must have been in opposite chromosomes, whereas in the previous cross they were in the same chromosome.

If we test the F_1 females by mating to black vestigial males, four classes result, viz.,

Non-crossovers		Crossovers	
Black, long	Gray, vestigial	Black, vestigial	Gray, long
41.5 per cent.	41.5 per cent.	8.5 per cent.	8.5 per cent.
83 per cent.		17 per cent.	

Crossing over has taken place in the F_1 females, and the numerical results show that this happens in

17 per cent. of cases. Here too we see that now the factors tend to separate, whereas in the case of the other F_1 female they tended to stay together, since they lay in the same chromosome. In the present case, when the chromosomes interchange, the factors are brought together, and so the crossover classes are just the opposite in the two cases, as also are the non-crossover classes. Yet there is the same amount of crossing over shown in both crosses, so that the frequency of the double recessives and double dominants in the first cross is exactly equal to the frequency of the single recessive and single dominants in the last cross. Which classes shall have the high frequency and which the low does not depend on the nature of the factors themselves, therefore, but on which ones come from the same parent, *i.e.*, lay in the same chromosome at first, and which lay in opposite chromosomes. *The amount of crossing over is seen to be independent of the way in which the factors enter an individual.* Hence it is fair to infer that the process is not peculiar in any way to hybrids, but takes place in the same way and to the same extent in gametogenesis in pure homozygous stocks. This is also indicated by the fact, later to be discussed, that when several different allelomorphs of a factor may occur, all give the same per cent. of crossing over with other factors.

Many other combinations, involving a large number of different characters in the second group, have been studied and give consistent results. There is never any crossing over in the male; and, in the fe-

male, the amount of crossing over is different for different factor combinations, but, for any given combination, it is not altered by the way in which the factors entered the cross, and is, ordinarily,[1] constant.

Tests like the preceding ones for the second group have been carried out for the third group, and give the same kind of results. There is crossing over in the female and no crossing over in the male.

In the fourth group, where only three factors are known, it is found that there is no crossing over between them in the male, and only a very slight amount in the female.

In the first group (sex linked characters), a very large amount of data has been collected. Here again there is abundant evidence to show that crossing over takes place in the female, but not in the male. The curious fact also comes to light that no mutations have been discovered in the Y chromosome, nor does it contain any factors dominant to any known mutant or normal factors in its mate, the X chromosome. Since the linkage of a considerable number of factors in the X chromosome has been studied in detail the evidence from this source best serves to illustrate cases where the linkage is strong, where it is moderate, and where it is weak.

The body color called yellow and the eye color white have been used in many experiments. If a yellow white female is mated to a wild male (gray red) (Fig. 23), the daughters are gray with red eyes (like the fathers), but the sons are yellow white like

[1] Subject to certain variations which will be noted later.

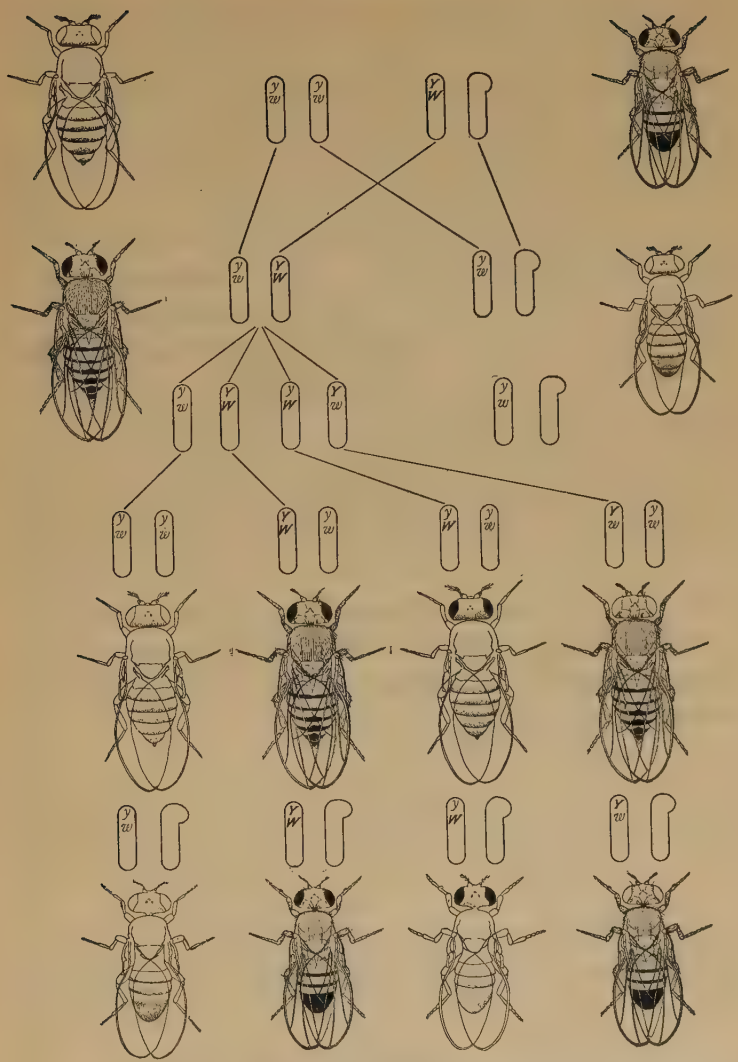


FIG. 23.—Diagram illustrating the inheritance of two pairs of sex-linked characters, viz., yellow white and gray red. In F_2 the males and the females are of the same classes.

the mother. The explanation of this result is obvious; for the son gets his single X chromosome from his mother, and should therefore have the characters that go with this chromosome. His Y chromosome, derived from the father, does not influence the result at all. The daughters, however, get one X chromosome from the mother (yellow white) and the other from the father (gray red). The factors for gray and red dominating give gray red daughters.

The composition of these F_1 females can be tested by breeding to the double recessive male (yellow white) since this does not carry any dominant factors which will obscure what factors are received by the F_2 females from their mothers. But the F_1 males are themselves yellow white, so that the F_1 females may be mated to their brothers. In fact, the outcome is the same, whether a yellow white male from stock or a yellow white F_1 brother is bred to the F_1 female. The F_2 offspring of such crosses give the following classes and ratios:

Non-crossovers		Crossovers	
Yellow white	Gray red	Yellow red	Gray white
49.5 per cent.	49.5 per cent.	0.5 per cent.	0.5 per cent.
99 per cent.		1 per cent.	

This F_2 result reveals the kinds of eggs produced by the F_1 female (since a double recessive father was used). Crossing over takes place between yellow and white in only 1 per cent. of cases.

There is no way of testing linkage in the F_1 male, which is like a homozygous individual so far as the re-

sult is concerned, as his Y chromosome does not contain any factors dominant to yellow and white, even though it came from the gray red male.

The reciprocal cross also offers certain points of interest. When a gray red female is mated to a yellow white male both sons and daughters are gray red. The daughters get a gray red chromosome from the mother and these factors dominate the factors derived from the father. The sons (F_1) get their single X chromosome from their mother and show her colors (gray and red).

If these gray red F_1 females are back crossed to a yellow white male they give the same numerical result that this test gave in the reciprocal cross, viz., four classes of offspring with 1 per cent. of crossing over.

The F_1 males behave in all crosses exactly as do wild males, which is to be expected, since their single X chromosome is derived from the wild type mother.

It will not be necessary to consider in detail the same cross when the two factors enter from different parents; they will now keep apart exactly to the same degree that they kept together before. This is illustrated for the backcross as follows:

Non-crossovers		Crossovers	
Yellow red	Gray white	Yellow white	Gray red
49.5 per cent.	49.5 per cent.	0.5 per cent.	0.5 per cent.
99 per cent.		1 per cent.	

As pointed out in the discussion of the black vestigial cross, this fact is very important, for it serves to

show in a most striking way that in the previous experiment with yellow and white, these factors hold together so strongly from generation to generation, not because of any innate relation between these characters, but simply because they started together in the same chromosome.

In the case of yellow and white just given the linkage between the two factors is very strong in the sense just defined, that is, they tend in a high degree to preserve whichever combination they have. Other factors show a different strength of linkage. For example, if a female with white eyes and miniature wings is bred to a wild male, and then the F_1 females (red, long) are backcrossed to white miniature males they will give the following classes of offspring.

Non-crossovers		Crossovers	
White miniature	Red long	White long	Red miniature
33.5 per cent.	33.5 per cent.	16.5 per cent.	16.5 per cent.
67 per cent.		33 per cent.	

The two large classes, white miniature and red long, correspond to the combinations that entered. The two smaller classes are the crossover combinations. Crossing over, therefore, takes place in 33 per cent. of cases.

Another combination gives a still greater amount of crossing over: the linkage may be said to be weaker. If a white eyed female is bred to a bar male (bar is a dominant mutation), and if the F_1 females (red bar eyed) are bred to the double recessive (white round eyed) sons, the following classes appear:

Non-crossovers		Crossovers	
White round	Red bar	White bar	Red round
28 per cent.	28 per cent.	22 per cent.	22 per cent.
56 per cent.		44 per cent.	

Here a large amount of crossing over appears, about 44 per cent. In fact, so freely do the factors interchange that without sufficiently large and accurate numbers the linkage might entirely escape detection.

The Mechanism of Crossing Over

If it be admitted that the Mendelian factors are carried by chromosomes it can not be denied that interchange between homologous chromosomes must occur, for sex linked factors cross over from each other, and yet are known to be in the same pair of chromosomes, since they all follow the X chromosome in its distribution. The evidence allows for no other interpretation. But why should crossing over take place so rarely between certain factors and so often between others? We can make use here of certain information in regard to the chromosomes that gives a very simple answer to the question. In the early germ cells, before the maturation period begins, the chromosomes appear to be scattered in the nuclei, and the homologous chromosomes in many cases show no tendency to lie together, although in some animals, *e.g.* in many flies, the members of a pair are often found side by side. In this early period the germ cells divide as do other cells and thereby increase in numbers. But at the termination of this

period, the homologous chromosomes unite in pairs. There has been much controversy as to how this union takes place, but in some cases at least, the uniting chromosomes twist around each other as they come together. This is illustrated to the left in Fig. 24. As a consequence, parts of one chromo-

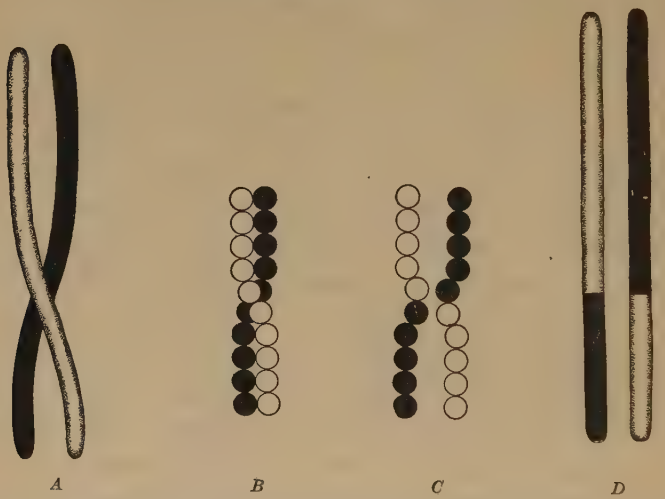


FIG. 24.—Diagram to represent crossing over. At the level where the black and the white rod cross in *A*, they fuse and unite as shown in *D*. The details of the crossing over are shown in *B* and *C*.

some will come to lie now on one, now on the other side of the mate. If when the twisted chromosomes separate, the parts on the same side go to the same pole the end result will be that shown to the right in Fig. 24. Each chromosome has interchanged a part with its mate. This process has been called crossing over. It is, of course, also possible that the twisted chromosomes do not break and reunite where

they cross, and if they do not then when they begin to separate they simply pull apart irrespective of the side on which they lie. When this occurs each chromosome remains intact and no crossing over takes place.

Later some of the evidence on which the above statements rest will be examined more critically. For the present it need only be pointed out that such a crossing over of parts of the chromosomes would supply the necessary mechanism to account for interchange. If the crossing over may occur at any point in a chromosome, then the chance of its occurrence between two given loci will be greater, the greater the distance between those loci. If then the Mendelian factors lie along the chromosomes, the amount of crossing over between any two of them will depend on their distance apart. Should two points lie near together a crossover will only rarely occur between them; if they lie further apart the chance of such a crossover taking place at some point between them will be greater. From this point of view the percentage of crossing over is an expression of the "distance" of the factors from each other.

In this way the diagram shown in the frontispiece has been constructed. Not only can all the facts of linkage so far studied be explained on this basis, but, as will now be shown, certain further results can be predicted. This is illustrated in what may be called a three-point experiment, *i.e.*, an experiment in which three pairs of factors are involved.

The three factors already studied, namely, white, miniature, and bar, furnish an excellent illustration. If we represent the percentages of crossing over as relative distances along the chromosome the three points will lie as shown in Fig. 25.

If crossing over takes place between white and miniature and between miniature and bar, then it

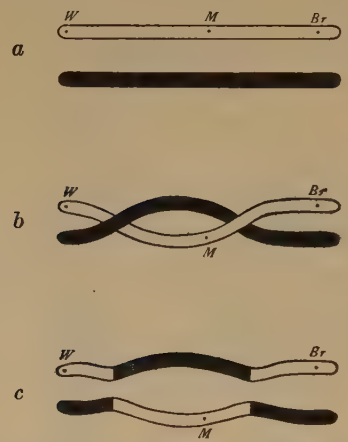


FIG. 25.—Diagram to illustrate double crossing over. The white and the black rods (*a*) twist and cross at two points. Where they cross they are represented as uniting (shown in *c*). That an interchange of pieces has taken place between *W* and *Br* is demonstrated by the factor *M* having gone over to the other chromosome.

might be expected sometimes to take place in both regions at once, as shown in Fig. 25, *b*. The result here would be to produce two chromosomes like those shown in the lower figure. The combinations of factors which these two chromosomes resulting from double crossing over would contain, are white long bar and red miniature round. Since these two classes

of gametes are actually produced, the results of the experiment fulfil the theoretical expectation.

There is a corollary of importance to this conclusion. When a cross is made that involves only white and bar, the double crossing over, that can be detected only when an intermediate point is followed, must still be supposed to take place. Whenever it does take place white bar flies and red round flies result. These will be added to the non-crossover classes since they have the same external characteristics. Hence the apparent non-crossover classes will be increased and the crossovers decreased, so that the sum of the value for *W* and *M* (33) and that for *M* and *B* (22) is much greater than the value for *W* and *B* (44) observed when only these two factors are involved. Here then we have an explanation of why long distances taken as a whole give too little crossing over, as compared with the same distances taken section by section. The lowered percentage is an actual mathematical necessity owing to the occurrence of double crossing over.

In the case of double crossing over the two points of crossing over can not be near together unless the chromosomes are tightly twisted. Consequently, when crossing over occurs at any point the region on each side should be protected from further crossing over. That this actually happens may now be demonstrated. For example, from vermilion to sable is 10 units, and from sable to bar is 14 units more (as seen in frontispiece). When crossing over occurs between vermilion and sable the region between

sable and bar should be somewhat protected from crossing over. The usual amount of crossing over between sable and bar is 14 per cent., but in those cases in which crossing over between vermilion and sable occurs, this value becomes reduced to somewhat less than 4 per cent. In this same fashion a region just to the left of sable is protected, but this protection decreases with the distance from the vermilion sable region. The fact that one crossing over makes less likely another crossing over in a nearby region, or in a sense *interferes* with a second crossing over nearby, is called *interference*. It is found that interference decreases with increase of distance until, in group I, it vanishes at a distance of about 46; *i.e.*, a crossing over at one point does not affect the chance of crossing over at another point 46 units away. Weinstein finds, however, that at a still greater distance interference reappears, so that there is a modal distance between the two breaks in double crossing over, possibly due to the threads bending in loops that tend to have a certain length.

In the chromosome maps the distance taken as a unit is that within which 1 per cent. of crossing over occurs. Thus yellow and white are 1.5 units apart in the frontispiece, since there is 1.5 per cent. of crossing over between them. White and bifid give 5.5 per cent., hence are placed 5.5 units apart, and since yellow and bifid give 7 per cent., bifid must be placed on the other side of white from yellow. The other factors have been plotted similarly, each locus being determined, as far as possible, by

the per cent. of crossing over between it and the factor nearest to it. For shorter distances it may be said that the number of units on the map between any two factors (A and C), will equal the per cent. of crossing over that will actually be observed between them in an experiment involving these two pairs of factors, even although their distance on the map may not have been obtained directly from their linkage with each other, their positions having, instead, been determined by their linkage with other factors. On account of double crossing over, however, this would not be expected to hold for the longer distances; and, as has been explained, we do actually find that, if long distances are involved, the distance between A and C determined as on the map, by adding the intermediate distances A–B and B–C, is longer than the distance AC as directly determined in an experiment involving only these two pairs of factors. It nevertheless remains true that, given the distance between any two factors on the map, the per cent. of crossing over between them can always be *calculated* from this distance (since the amount of discrepancy due to double crossing over also depends on the distance); this shows that the amount of crossing over between them is an expression of their position in a *linear series*. This striking fact, that the mathematical relations between the various linkage values conforms to a linear series, is a strong argument that the factors are actually arranged in line in the chromosomes. If the relations between the various linkage values were not determined by some linear relation of the

factors but were of a random sort, these relations could not be calculated from a linear map.

As a concrete illustration of the way in which a group of factors behaves as a linear series, attention may be called to the manner of distribution of the factors among the germ cells of a female heterozygous for a large number of factors in the same pair of chromosomes. Let us write the factors derived from one parent, *i.e.*, those in one of the chromosomes, on one line (see formula p. 67), in the order which they have on the map (see frontispiece), and the allelomorphic factors derived from the other parent, *i.e.*, those in the homologous chromosome, in corresponding positions on the line below. Then in such a case the mature eggs contain either all of the factors represented on one line and none of those on the other, or they contain all of the factors present in one *section* of the line, and all of the factors present in the remaining section of the other line. In other words, the factors obviously stick together in sections according to their position in the linear series. When double crossing over occurs the line is broken in two places, but even here whole sections remain intact.

The above facts may be illustrated by an actual case. The first formula shows the composition of a hybrid female which has received from her mother the mutant factors: yellow, white, abnormal, bifid, vermilion, miniature, sable, rudimentary, and forked, and from her father the normal allelomorphs of these factors, together with the dominant mutant factor, bar.

$$\left\{\frac{y\ w\ a\ b_i\ v\ m\ s\ r\ f\ b'}{Y\ W\ A\ B_i\ V\ M\ S\ R\ F\ B'}\right\}$$

A number of females of this type have been made up by Muller. The next formula shows the kinds of eggs that were produced by one of these females and the numbers of each kind that were produced.

Non-crossovers:

y w a b_i v m s r f b′ – 6.
Y W A B_i V M S R F B′ – 8.

Single crossovers:

Y W a b_i v m s r f b′ – 2.
Y W A B_i v m s r f b′ – 2.
y w a b_i V M S R F B′ – 2.
Y W A B_i V m s r f b′ – 1.
Y W A B_i V M S r f b′ – 1.
y w a b_i v m s R F B′ – 1.

Double crossover:

y w a b_i V M S R F b′ – 1.

Counts of over 600 offspring from females of the same type have given similar results. The characteristic method of interchange here demonstrated may perhaps be better realized by contrasting the combinations just given with the following, which illustrate types of eggs found *not* to be produced by such females:

y W a B_i V m S r f B′
Y W a b_i V m s R f B′

It is not supposed, however, that the per cent. of

crossing over represents precisely the distance between the factors, for it may be that crossing over is more likely to take place in one region of the chromosome than in another. In that case the distances between factors in this region calculated from the amount of crossing over between them, would be relatively greater than the actual distance. It is supposed, however, that at least the order of the factors in the diagram represents their real order. Sturtevant has found definite factors which alter the amount of crossing over in the chromosomes, and these factors actually do affect the amount of crossing over differently in the different regions. A map of the chromosomes based upon the per cent. of crossing over when these factors are present would show different relative distances between the loci than those calculated from the normal linkage values. It is to be noted, however, that even in these diagrams, the *order* of the factors remains unchanged. One of the factors lies in the second chromosome and lowers the amount of crossing over in certain regions of this chromosome; the other lies in the third and apparently affects only this chromosome, and chiefly the end of this chromosome in which it itself is located. Bridges has found that the percentage of crossing over in the second chromosome is also lowered with increase in the age of the female, and Plough has found that temperature as well may affect the amount of crossing over. This variation in crossing over is in no way prejudicial to the conception of crossing over above outlined. Variation in the amount of crossing over has

also been found in other forms than Drosophila, but in these cases the determining conditions and their effect on the various linkage values have not as yet been discovered.

Linkage in Other Animals and in Plants

Since the discovery in 1906 of linkage in sweet peas many cases have been found in animals and in plants. In sweet peas themselves two groups of linked factors are now known, one containing three pairs of factors and the other three or possibly four. In garden peas there are two pairs of linked factors and two other cases that are doubtful; in the primrose there is a group of five pairs of linked factors; in the snap-dragon there is a group of three pairs; in stocks there is a group of three or probably four pairs. In animals, linkage, aside from sex linkage, has been discovered in several forms besides Drosophila, viz., in domesticated poultry by Goodale, in pigeons by Cole, in rats and mice by Castle, in the silk-worm moth by Tanaka, and in Apotettix by Nabours. There are, it is true, several other cases in which the evidence leads one to suspect that linkage occurs, but these are too uncertain at present to be included in the list. In all the above cases the linkage is "partial," that is, a certain amount of crossing over takes place, at least in one sex.

There are a number of cases of sex linkage, which, being only a special case of linkage, undoubtedly belong in the same category, but the amount of cross-

ing over between the sex factor and the various sex linked factors can not be calculated, since in the sex that is heterozygous for the sex factor no crossing over has been observed. Sex linkage has been found

FIG. 26.—Black Langshan female by Barred Plymouth Rock male. Compare with Fig. 30 (similar cross in Abraxas) for scheme of inheritance, which is the same in both. Substitute Black for lacticolor and Bar for grossulariata.

in the moths Abraxas (Figs. 30 and 31) and Lymantria, in the fowl (Figs. 26, 27, 28, 29) (six factors), canary, pigeon, Drosophila (Figs. 9 and 10), fish, cat, man, and the plant Lychnis. In all, somewhat more than fifteen species show linkage.

This number appears small in comparison with the

large number of species in which Mendelian inheritance has been discovered; but there are several reasons why more cases have not been recorded. In the first place, the number of chromosomes is generally large compared with the number of characters that

FIG. 27.—Barred Plymouth Rock female by Langshan male. Compare similar cross in Abraxas for scheme of inheritance.

have been studied in such a way that linkage would be noticed. Thus, there is little chance of finding two factors lying in the same chromosome. Secondly, unless this linkage is close, it might easily escape detection, especially when the number of off-

spring recorded is small. In such cases the data are usually fitted to the nearest "Mendelian" ratio even

FIG. 28.—Photograph of the P_1 (1 and 2) and F_1 (3 and 4) birds in such a cross as that of Fig. 26.

though discrepancies are apparent. Even in species where a number of different characters have been studied these are often recorded in separate tables,

which excludes the possibility of detecting any linkage that is present, for obviously linkage cannot

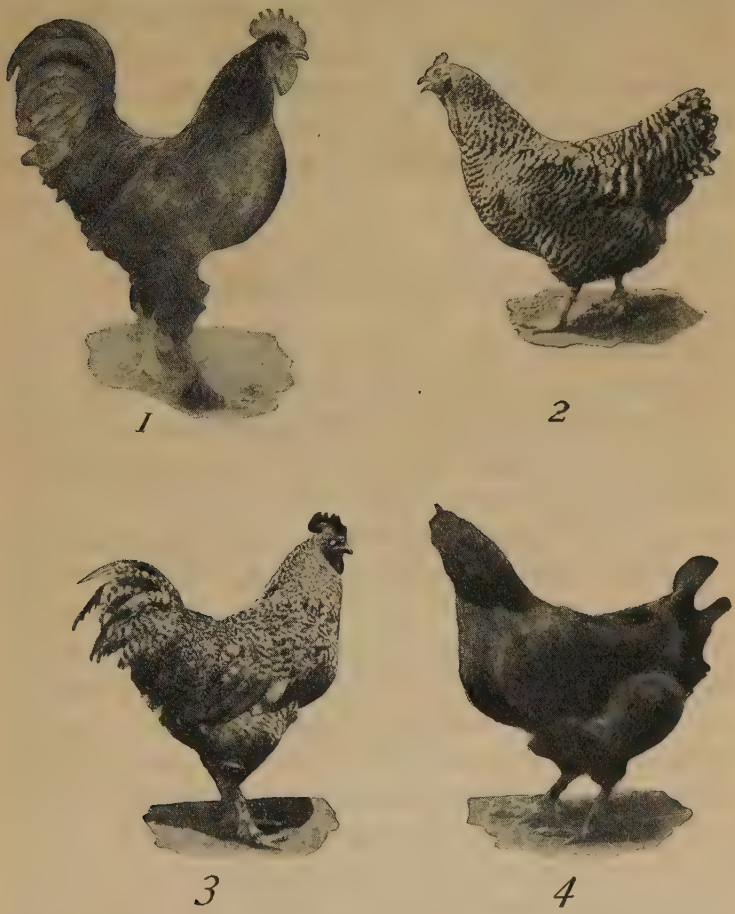


FIG. 29.—Photograph of P_1 (1 and 2) and F_1 (3 and 4) birds in such a cross as that of Fig. 30. The P_1 male is a standard figure.

be seen unless at least two pairs of factors are studied at the same time. The steady increase in the number

of cases of linkage that is occurring at the present time, when the importance of detecting them has become apparent, and the methods for studying them have been worked out, appears to presage the realization of linkage as a general phenomenon. Its occurrence in such widely separated types is also a sign that it is a constant accompaniment of Mendelian inheritance.

The Reduplication Hypothesis

Linkage has been interpreted by Bateson and his co-workers on a basis entirely different from that adopted in this book. These investigators do not connect Mendelian factors with the chromosomes in any way, and do not suppose that segregation occurs at the reduction division. In a case of linkage between two pairs of factors, Aa and Bb, the doubly heterozygous individual will have the formula ABab. Bateson supposes that in such an individual segregation takes place before the reduction division—perhaps in early cleavage stages, perhaps after the formation of the gonads. Two cell divisions are required for this segregation. In the first, *A* and *a* do not divide, but one goes to each daughter cell, *i.e.*, they segregate. B and b, however, both divide, and each daughter cell receives both B and b. The resulting cells then have the formulæ, ABb and aBb, respectively. In other words, A and a have segregated, but B and b have not. At the next division B and b segregate, giving four cells, with the combina-

tions AB, Ab, aB, and ab, respectively. These cells then proceed to divide, the number of divisions not being the same for each, which results in the production of more of some kinds of cells than of others. But this multiplication must be assumed to be a symmetrical process, since the observed number of AB gametes equals the number of ab, and similarly Ab equals aB. The whole process just described is known as "reduplication." The term is applied to the same cases as those included under the name of linkage.

When three pairs of factors are involved in the same "reduplication series" Bateson supposed at one time that they are segregated at three successive cell divisions, after which the eight resulting cells divide at unequal rates. Later Trow suggested for such a case that perhaps only two segregating divisions occur at first, producing the cells ABCc, AbCc, aBCc, and abCc, which may then multiply so as to give the proper proportions for the A and B combinations. After this there occurs in every cell a division which segregates C and c. The resulting cells then divide again so as to produce the observed relations between the C pair and the other factors.

The nature of the factors themselves in the different lines of cells resulting from segregation can not be supposed to determine the difference in the number of times that these lines divide, because if an individual has received AB from one parent and ab from the other, the lines of cells reduplicate in a way just opposite to that in an individual which received Ab

from one parent and aB from the other. In one individual the line AB divides a certain number of times more than aB, whereas in the other aB divides just that many times more than AB. In other words, the number of times a line of cells divides must be assumed to be determined in some way by whether or not, in its formation, certain factors separated that had established a relation with each other by being present together in the egg or sperm from which the individual came. To explain this, Bateson and Punnett have suggested that at the time of fertilization there is established in the egg a "polarity" which determines the planes of the segregating divisions. But it seems impossible to imagine how this or any other mechanism could bring about the above result. On attempting to follow out in concrete detail the events which must be assumed to occur in any case of reduplication, we find that, if the above stated relation is to hold, then, on "polarity" or any other hypothesis, the assumption of the most intricate and improbable relations and processes is forced upon us.

This interpretation of linkage was originally based largely upon the supposed fact that the "gametic ratios" (ratio of parental combinations to new or crossover combinations in the gametes) fell into the series 1:1:1:1, 3:1:1:3, 7:1:1:7, 15:1:1:15, 31:1:1:31, etc. The supposed connection between this series and reduplication is too involved to explain here, and gametic ratios which do not fall into it are now definitely known. In fact, it seems probable that

ratios which do fall into it are no more frequent than would be expected from a chance distribution.

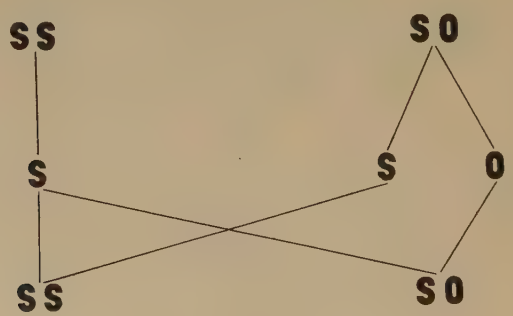
Another assumption upon which the reduplication hypothesis is based is the old idea of somatic (pre-reductional) segregation. This hypothesis, once advocated by Roux and Weismann as an explanation of differentiation, is opposed by a large body of experimental evidence from the fields of regeneration and experimental embryology, and has been given up by practically all students of developmental mechanics, including Roux himself. Altenburg's crosses of Primula proved segregation of the linked factors to occur after gonad formation. In flies Plough found heat to affect linkage only if applied after the completion of most, if not all, the gonial divisions that might have "reduplicated" the eggs in question.

At first it was doubted whether more than two pairs of factors could show reduplication in the same organism, but when it was experimentally proven that two pairs were not the limit, the scheme was extended. When gametic ratios not falling into the 3, 7, 15 series were found, the theory was modified to permit other ratios. When it was found that the result depended upon the way in which the factors entered the cross, the "polarity" hypothesis was added. Some further extension would be necessary to account for interference. That interference is a widespread phenomenon is shown by its occurrence in Altenburg's Primula crosses, and in those of Anderson on corn—the only crosses outside of Drosophila giving the exact relations of more than two factors.

CHAPTER IV

SEX INHERITANCE

There are two types of sex inheritance known in those species in which separated sexes exist. In one type, which may be called the Drosophila type (XX-XY type, or, for short, the XY type), the female is homozygous for a sex factor, the male heterozygous; in the other, the Abraxas type (the WZ-ZZ type, or, for short, the WZ type) the female is heterozygous for a sex factor, the male homozygous. Since in both cases the heterozygous individuals must always mate with the homozygous ones there should result in each succeeding generation equal numbers of heterozygous and homozygous individuals, and so the bisexual condition is perpetuated as follows:



The genetic evidence so far gained has placed in the Drosophila type the following animal forms: Dro-

sophila, man, cat; and the plants, Lychnis and Bryonia. The cytological evidence refers to the same type the insect groups of bugs, flies, beetles, grasshoppers; the spiders, certain worms (Ascaris), echinoderms, amphibia and mammals (including man). The genetic evidence has placed in the Abraxas type several moths and butterflies, and several birds; viz., chickens, ducks, and canaries.[1] Favorable cytological evidence has been found only in the case of a few moths.

In many cases of the Drosophila type, in which the history of the sex chromosomes has been worked out cytologically, it has been found that in the male there is a pair of chromosomes, the two members of which are different in size or shape. These are the "sex chromosomes" and are designated as X and Y. In many species of the Drosophila type the Y is slightly smaller than the X, and in the various other species of this type all gradations in the relative size of the Y are found, between this condition and the condition where Y is completely absent. In some related species, on the other hand, the chromosomes which obviously correspond to X and Y are alike in appearance. It is not, after all, the size difference usually visible in the male, between X and Y, which gives these two chromosomes their significance in sex determination, but rather a difference in the factors they contain. The size difference is an incidental concomitant, or, as it were, a token or label that is

[1] Richardson's work on strawberries suggests that this plant may come under the Abraxas type.

not present in all species. In all these cases the female contains two X chromosomes, the Y chromosome being confined to the male line.

This type of sex determination represents all eggs as alike—each containing one X (after the polar bodies have been extruded), but the sperm is of two kinds, one containing the X and the other Y, or merely no X. The scheme is as follows:

It will be seen that all the spermatozoa carrying X produce females, while all those carrying Y or no X produce males.

The Y chromosome, when present, descends from father to son. It might seem, therefore, that if the Y carried a sex factor for maleness the scheme would work out as well as if a sex factor were carried by the X chromosome. But in several cases there is no Y in the male, and in certain cases to be described later, due to non-disjunction, there are females that have a formula XXY and yet their sex is not affected in any way on account of the presence of the supernumerary Y. It follows that sex is not determined by the presence or absence of the Y chromosome but by the

number of the X chromosomes that are present. In the cases that follow, where sex determination of the Drosophila type was discovered by a study of sex linked inheritance, as well as in the above cases, where the mechanism was discovered through cytological observations, proof that the male is heterozygous for a *Mendelian factor* for sex is derived from the fact that he gives rise to two kinds of spermatozoa—male producing and female producing—in equal numbers. We know this in the cases worked out cytologically because here the spermatozoa carrying X must all produce females, while the other half must produce males; and we know it, in the cases worked out genetically, because here only half the spermatozoa from a male with a dominant sex linked character carry the dominant factor, and these all produce females, while the rest produce males. The female must contain the same Mendelian sex factor as is present in the female-producing spermatozoa of the male; but the female must be homozygous for this factor, since any egg, if fertilized by a male-producing spermatozoon, contributes this factor to the resulting male.

Although the only way in which the results of sex linked inheritance of the Drosophila type differ from non-sex linked cases is the one above stated, namely, that a dominant male transmits his dominant sex linked factor only to his *daughters*, nevertheless it may be well at this point to recall specifically what ratios are produced in consequence, in the various types of crosses.

Examples of sex linked inheritance in Drosophila

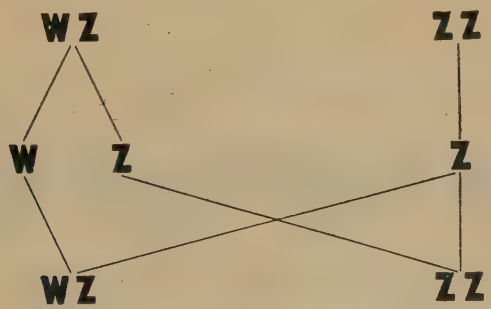
have already been given; that of white eyes is typical of all the rest. The main facts may be restated here. If a white eyed male is bred to a red eyed female the offspring are red eyed (Fig. 9). If these are inbred all of the F_2 daughters are red eyed, but half of the sons are white eyed and half red eyed. In a word, the grandfather transmits his characters visibly to half of his grandsons but to none of his granddaughters.

In the reciprocal cross (Fig. 10), a white eyed female bred to a red eyed male produces the criss-cross result of red eyed daughters and white eyed sons. These give white and red eyed males and females in equal numbers. On the assumption that the factor for white eyes is carried by the sex chromosomes the inheritance of white eyes can be readily understood. It will be observed that a female transmits to each of her sons one of her X chromosomes with all the factors contained in it. Her sons will show all of these sex linked characters whether they be dominant or recessive since they receive no other X to dominate those characters and the Y contains no dominant factor. For example, if a stock be made up pure for yellow body color, white eyes, abnormal abdomen, bifid wings, sable body color, forked spines and bar eyes, and if such a female be bred to a wild male, all of her sons will be yellow, white, abnormal, bifid, sable, forked and bar. The daughters, however, will receive not only this chromosome from their mother, but will also receive a chromosome from the wild male (their father) con-

taining the normal allelomorphs of all these factors. In the case of all the factor-pairs, except abnormal and bar, the normal allelomorph dominates. Therefore, the females will appear normal for all characters except abnormal and bar, which are dominant.

In the cat, Doncaster and Little describe a sex linked factor affecting the color. In man several characters, such as color blindness, hæmophilia, and others less certainly identified have been found to follow the same scheme.

A comparison of sex linkage in Abraxas with that in Drosophila shows that the mode of inheritance of sex linked characters is identical in these two cases, but the sex relations are exactly reversed. In the Abraxas type sex linked inheritance takes place in accord with the plan that the female is heterozygous in sex production. If the chromosome that carries this sex differentiator is called Z, and its mate in the female W, the formula for the male would be ZZ and that for the female WZ. The scheme follows:



Inheritance in Abraxas is illustrated in the following diagrams (Figs. 30 and 31), in which the common

wild type A. grossulariata is crossed to the rare mutant type A. lacticolor.

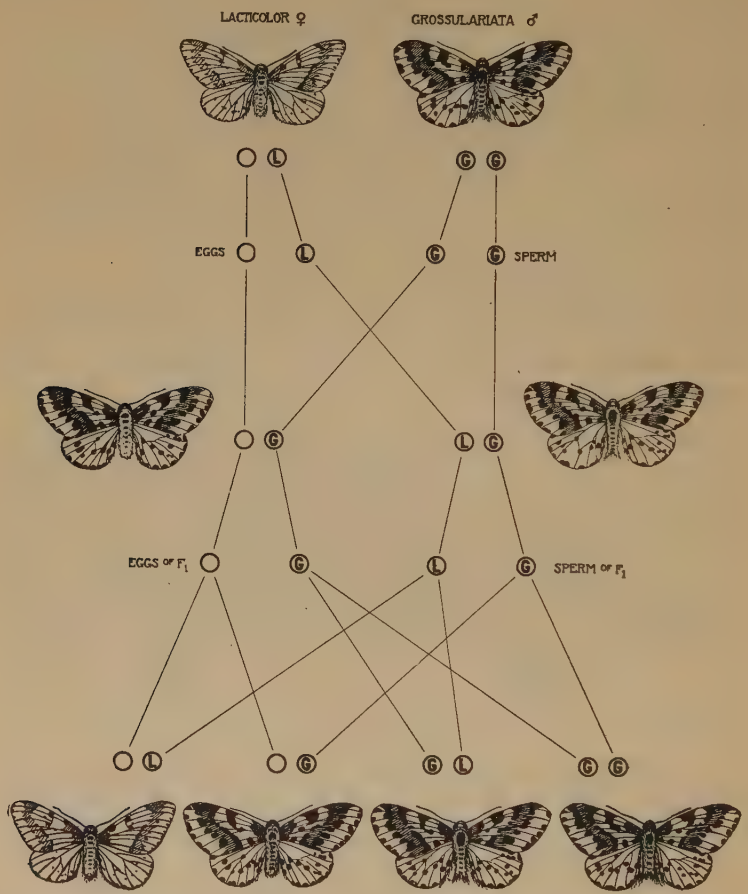


FIG. 30.—Abraxas lacticolor female by A. grossulariata male. The sex chromosomes are represented by the circles in the center of the diagram, and the letters contained in them stand for the factors that each carries. The W chromosome, confined to the female line, is represented without either L or l; for it, like the Y chromosome in Drosophila, carries no sex linked factors.

In the first cross (Fig. 30), where the lacticolor female is mated to the grossulariata male, the off-

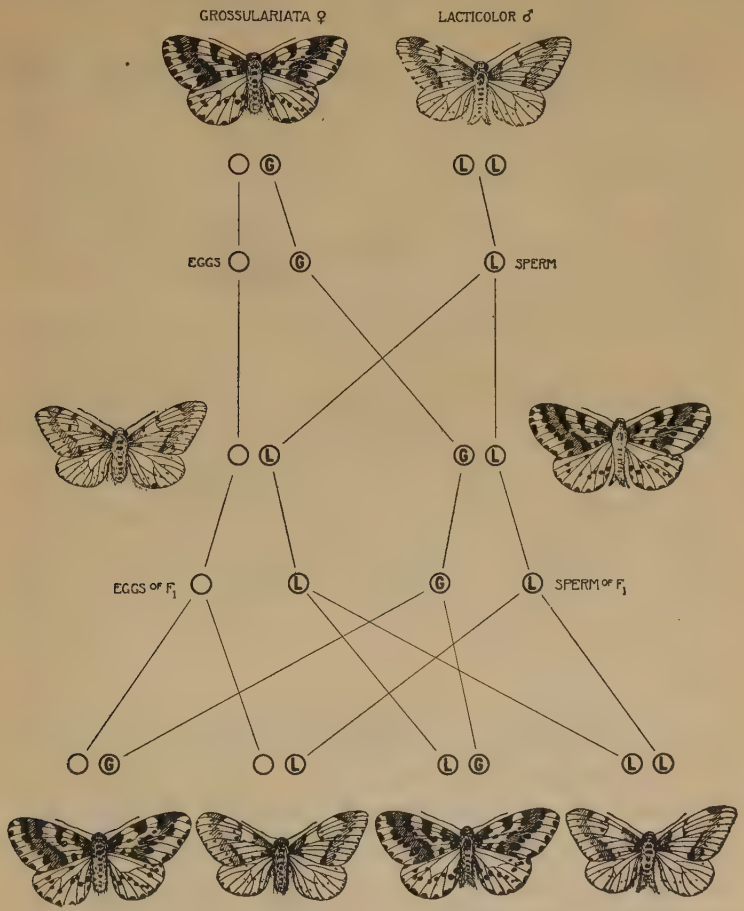


FIG. 31.—Abraxas grossulariata female by A. lacticolor male. The reciprocal cross of the one shown in Fig. 30.

spring are all of the grossulariata type. When these are inbred they give (F_2) three grossulariata to one

lacticolor, but the lacticolors are females only. The lacticolor grandmother has transmitted her peculiarity *visibly* to half of her granddaughters, but to none of her grandsons.

In the reciprocal cross (Fig. 31) of lacticolor male by grossulariata female, the daughters are like their father (lacticolor), and the sons are like their mother (grossulariata). This is so-called criss-cross inheritance. When the hybrids (F_1) are inbred, they give lacticolor males and females and grossulariata males and females in equal numbers.

Sex linked inheritance, as shown by the foregoing results, becomes intelligible if the factor for lacticolor is carried by the chromosome Z. Its occurrence in Z is indicated here by writing an l inside the circle which represents that chromosome, while the allelomorphic character carried by the Z of the grossulariata individual is indicated by writing L in the circle. The W chromosome is indicated by the blank circle. The two cases then work out as shown in the diagrams.

The preceding analysis shows that the genetic evidence calls for a mechanism in which the female is heterozygous for sex, since those of her eggs which carry the factor for grossulariata all develop into females, the others into males. In the case of Abraxas there was for some years no positive cytological evidence in support of this view. Fortunately, the cytological side is now in a much better position owing to the work of Doncaster and Seiler.

Doncaster examined Abraxas cytologically, and

found that both the female and the male have 56 chromosomes, with no obviously unequal pair.

Normally in Abraxas the sex ratio is about 1 to 1. In one exceptional line this equality of sexes was not the rule. In this strain Doncaster found many females which gave only daughters, and not a single son. Other females of this line gave many daughters but also a few sons, while still others gave practically a normal 1 to 1 ratio.

When Doncaster examined this line cytologically, he found that although the males were normal, with 56 chromosomes, the females were aberrant, having only 55 chromosomes.

In the maturation of the eggs of such a 55 chromosome female, the odd chromosome went to one pole, so that one polar plate had 27 and the other 28 chromosomes. Doncaster first thought that the odd chromosome went more often to the polar body than to the egg, and that eggs that eliminate the odd chromosome become after fertilization individuals with 55 chromosomes, that is, females — while the few that retain it become 56 chromosome individuals — that is, males. Later work showed that the egg is left with 28 as often as 27 chromosomes. This result upsets the earlier interpretation.

In normal strains there is a W chromosome present, but since this W chromosome may be absent without effect upon the sex of the individual, as shown above, it must be regarded as functionless in determining sex, and in this sense it corresponds to the Y of Drosophila. This evidence proves that there is

present in Abraxas that cytological basis which the evidence from sex linkage demands, namely, a condition the converse of that known in other groups of insects.

The evidence that Seiler has obtained relates to the wild strains of the moth Phragmatobia fuliginosa. The reduced number of chromosomes in the polar plate of the egg is 28 (Fig. 32, *a*). The large dyad formed by synapsis of the sex chromosomes Z and W is shown in the middle of the group. At the first polar division all the chromosomes separate from their mates, the ordinary chromosomes (autosomes) as well as the sex chromosomes. But as W separates from Z, it breaks into two parts which we may call large W and small w (Fig. 32, *b*, *c*). As a result there are 29 chromosomes at one pole (the pole that contains W and w) and 28 chromosomes at the other pole (the pole containing Z). It is a matter of chance which group goes into the polar body and which remains in the egg. Consequently there are two kinds of eggs, Ww and Z.

In the male there are 56 chromosomes, which give the reduced number 28. The two large Z's can be made out in Fig. 32, *d*. These meet, when the reduced number 28 is formed, and then separate, one going to each pole (Fig. 32, *h*). Each spermatozoon contains, therefore, one Z chromosome.

FIG. 32.—Phragmatobia fuliginosa. *a*, equatorial plate of first polar body of egg; *b* and *c*, daughter plates of the first polar spindle; *d*, equatorial plate of spermatogonium; *e*, equatorial plate of first spermatocyte; *f* and *g*, equatorial plates of second spermatocyte; *h*, anaphase stage of first maturation; *i* and *j*, equatorial plates of somatic cells with 56 (in *i*), and 61 chromosomes (in *j*). (After Seiler.)

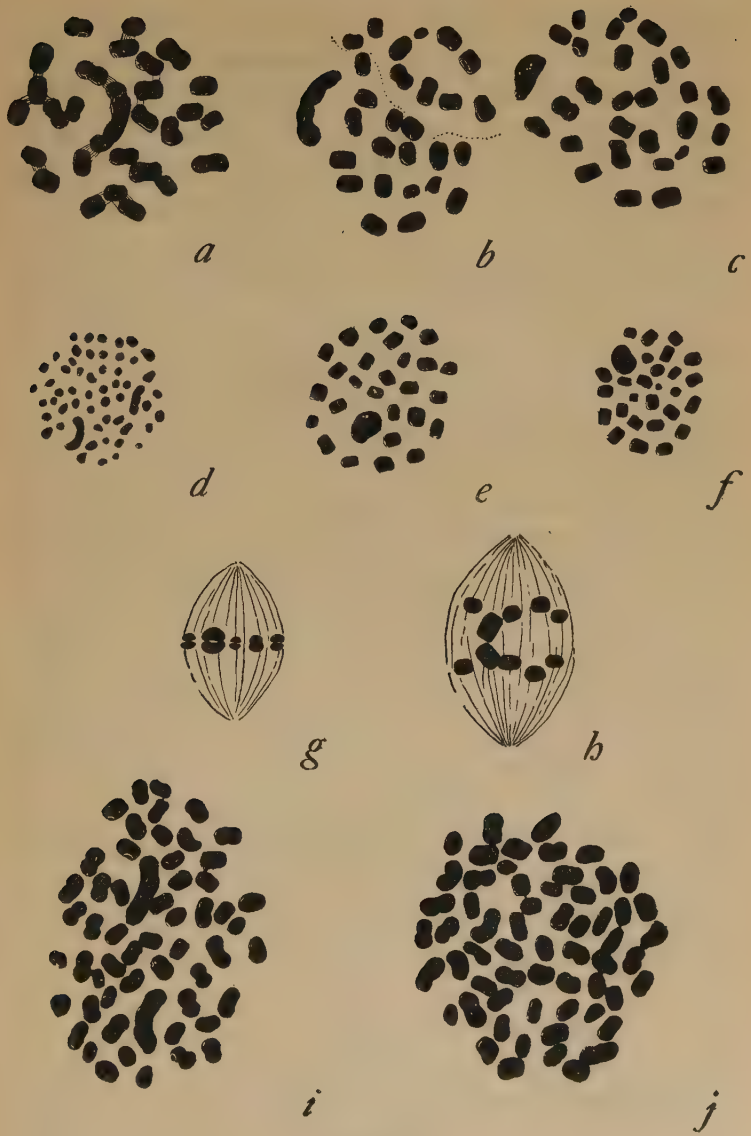


Fig. 32.

Any sperm fertilizing an egg containing Ww produces a female. The male embryos should contain therefore 56 chromosomes, the female 57. Counts of chromosomes in embryos show that while some contain 56, others contain 58, 61 and 62. Seiler suggests that the Z element is a compound and sometimes separates into its four components in the somatic cells. Recently (1919) Seiler has demonstrated in two other moths a lagging chromosome that may go out or remain in the egg in the ratio of 1.36 to 1.

In other Lepidoptera, examined by Stevens, by Doncaster, by Dederer and by Seiler, the males and females have the same chromosome configuration. In other words, if a WZ pair is present in the female the members are of the same size, or so nearly of the same size that they cannot be distinguished. It will be recalled that in a few other insects, believed for other reasons to belong to the Drosophila type, the X and the Y chromosomes are of the same size. The failure to find two sizes of sex chromosomes in moths is, therefore, not an argument against the view that the female is heterozygous for a sex factor. On the contrary, it is to be considered only a fortunate circumstance that this difference in a sex factor is sometimes associated with a size difference in no way directly depending on the sex factor itself.

What are Sex Factors

The inheritance of sex is explained by one chromosome difference that distinguishes the male from

the female. It does not follow from this that there is only one sex factor involved that is carried by the sex chromosomes. The symbols used here, viz., XX–XY and WZ–ZZ, are intended primarily for the chromosomes, but also for the sex factors.

These formulæ for the Drosophila type and for the Abraxas type raise the question as to whether the postulated sex *factors* are identical in the two cases. The employment of different letters for the two types suggests, of course, that the sex factors may be different. And it is true that the two sets of letters are used to avoid an apparent paradox that appears if we use only X and Y in both cases. If this is done, XY on one scheme represents the male and on the other scheme the female. Nevertheless, for the present the employment of different letters need not necessarily mean that different factors for sex are present in the two great classes, for these reverse results may be due to the action of the same factor-difference in a different setting. For example, acid may be the color differentiator in a setting of a certain solution containing it and litmus (with one drop of acid the color being blue, with two drops red), but in a setting containing Congo red the same differentiator may produce just the opposite effects (one drop red, two drops blue). On the other hand, it is conceivable that the setting (litmus and acid) may remain the same and yet a reverse result be produced by having a different differentiator —alkali instead of acid.

Since genetics has at present nothing to offer that will decide the question as to whether another set of sex differentiators is present, or whether the same differentiators with a different setting are involved in these two cases, discussion is quite certain to be futile.

It may seem inconsistent to use the name of the chromosome as the symbol for the sex factor when dealing with the inheritance of sex, while in all other cases a factor representing a point in the chromosome is used to designate the special character under consideration. No doubt with this idea in mind, several writers have followed the practice of indicating the sex factor by a significant letter, such as F for femaleness and M for maleness. As the use of such letters often involves a question of interpretation, a brief consideration may be given to this matter. In the discussion that follows reference is made always to the Drosophila type, but exactly the same arguments apply to the Abraxas type.

1. It has been suggested, for example, that a factor for the male be added to the formulæ so that maleness may not appear simply as the absence of one factor for femaleness. Thus, in such formulæ as FMFM (♀) and FMM (♂) the factor for maleness is added to indicate that when a single amount of F is present the male factors produce the male. But since M's are distributed everywhere, the formula is little more than a concession to male vanity, for M is not here a differentiator. Moreover, the use of the letters MM is here unjustifiable because there is no ground

for supposing that maleness is due to one pair of factors. It must be due to a complex of many factors all of which are present in both sexes.

2. Since there is evidence to show in some cases that there is no sex factor in the Y chromosome, the factor or factors carried by X can have no mate in this sex, hence the allelomorph or allelomorphs must be 0. If one chooses to represent this zero by a small letter, by f or m for instance, there is no inconsistency in doing so, for there is in this instance the cytological observation to justify its use. It is, however, misleading to represent this 0 by M as has sometimes been done.

3. There is at present no evidence to show that there is only *one* factor for sex carried by each sex chromosome, however probable this may seem from other relations, for it has not been possible to determine the linkage relation of the sex factor or factors to other factors in the sex chromosome, because crossing over of like factors in the homozygous sex would lead to no visible effect, and in the heterozygous sex no crossing over takes place.

4. If in the formulæ FF (♀) and FO (♂) the letter F is interpreted as a factor for femaleness, the formula must not be construed as meaning that F may not also be a factor for maleness. For, as a matter of fact, *one* F factor may be essential to the production of the male. Therefore, until we get more definite information as to the existence of a single or of several factors for sex, and as to whether they are the same factors in the two types, and what the rela-

tion of F and M may be in hermaphroditic types, it is less inconsistent to use the symbols for the sex chromosomes as the symbols for the sex factors also, if it is at the same time recognized that the whole chromosome is not involved in determining sex.

Hermaphroditism and Sex

Typical hermaphrodites are individuals that ripen both eggs and sperm. They are found widely represented in the plant and animal kingdoms, whole orders and classes consisting almost entirely of such individuals. Self-fertilization may occur, as in many plants, but cross-fertilization between different individuals appears more often to take place. In addition to these typical cases, that call here for no further comment, there are cases in which the individual may ripen first its sperm and later its eggs (protandric hermaphroditism), or vice versa. There are also several cases in which, in the young stages, eggs (or egg-like cells) appear in a gonad that is found subsequently to function as a testis. In the amphipod crustacean, Orchestia gammarillus, Boulenger found that 198 out of 217 young males contained ova, or egg-like cells, in the testes. In the adult males these cells had almost completely disappeared. In the male harvestman (Phalangium) large cells, said to be eggs, have been found in the testes. In the testes of the young male frog of some species there are large egg-like cells in the testes just prior to the time of metamorphosis. They

subsequently disappear. In the toad there is a special enlargement at the anterior end of the testis, called Bidder's organ, that is composed exclusively of large egg-like cells. The cells of this organ may be the same as the scattered cells in the testes of the young frog, which also occur sometimes in the young toad. On the other hand the same organ is found also in the young female toad, lasting throughout the first year of her life. If it is an ovary in the male, then the female would be said to have two kinds of ovaries, one rudimentary the other functional.

In the lamprey (Petromyzon) the young males also frequently have cells in their testes that appear to be immature ova. Schreiner has shown that in the hagfish (Myxine) immature males have ova in their testes, while immature females have young sperm-cells in their ovaries. In this case the sexes cannot be distinguished until maturity.

Certain teleostian fish pass through similar conditions, but one teleost, Serranus, is described by Dufossé and others as a true hermaphrodite.

Whether the two following cases belong under this heading may seem questionable. According to H. N. Gould, the mollusc Crepidula plana is male in the juvenile stage and female in later stages. He finds that unless a young specimen is placed in the vicinity of a larger individual the testes and male genitalia fail to develop, and when the animal grows older it develops ovaries and oviduct. But in the presence of a larger individual the young

animal becomes and remains functionally male. According to Baltzer, if the free swimming embryos of the gephyrean worm, Bonellia, are isolated they become sexual females. If however a swimming embryo that is ready to settle down comes to rest on the proboscis of a female, it develops into a rudimentary but functional male. A few embryos in each culture that do not settle down show signs of becoming hermaphroditic. It has been suggested (Geoffrey Smith) that the parasitic males ("complementary males") of certain species of barnacles owe their condition to their surroundings, as in Bonellia.

The most important information relating to the chromosomes in hermaphrodites and unisexual forms is that discovered by Boveri and Schleip from the thread worm, Rhabdonema nigrovenosum. This species has two generations in its life cycle. One generation consists of parasitic hermaphrodites that live in the lungs of the frog, the other consists of free-living males and females. The hermaphrodites and the free-living females have 12 chromosomes. The males have 11 chromosomes. In the hermaphrodite, both eggs and sperm are produced in the same germ-tube. The egg after maturation has 6 chromosomes. In the hermaphrodite two classes of sperm are formed which, according to Schleip, have 6 and 5 chromosomes respectively (one X-chromosome having been lost at one division). The former fertilizing the egg produces a free-living female, the latter a male. In the free-

living male it must be assumed that the no-X sperm is non-functional. The X-bearing sperms would fertilize the eggs and produce the hermaphroditic females.

Parthenogenesis and Sex

In the animal kingdom there are several cases where a species reproduces for several generations by parthenogenesis, and, then, at the end of the chain, sexual forms appear. The rotifer, Hydatina senta, is the best illustration since the change can now be controlled (Whitney). This animal ordinarily produces parthenogenetic eggs (Fig. 33, *A*, *D*), which give rise to females. If fed on a pure diet of the protozoon, Polytoma, only these parthenogenetic females are produced in successive generations (Whitney, Shull). If the diet is changed to the green alga (Euglena) a female will then lay eggs that give rise to a new kind of individual—a male-producing female which is not externally different from its mother. If the male-producing female is not fertilized by a male, soon after hatching (B), she produces a large number of small eggs (E) that develop parthenogenetically into males (C), but if she is fertilized she produces a few large eggs with thick shells (F)—the resting eggs—that always become females. Hence the change in diet has caused the appearance of a new kind of individual that functions as a sexual female with the production of a few daughters, or as a partheno-

genetic female producing many sons, according to whether she has been fertilized soon after hatching or not. The nature of the change in this female is not known, but it is known that the small male-producing eggs extrude two polar bodies, thus be-

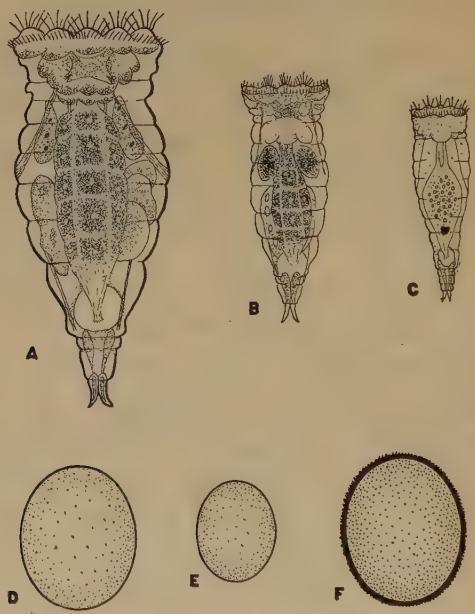


Fig. 33. — Hydatina senta. — *A*, the ordinary parthenogenetic female. *B*, sexual female, at time of hatching, when she is fertilized by the male. *C*, male. *D*, parthenogenetic female egg. *E*, parthenogenetic male egg. *F*, fertilized resting egg. (After Whitney.)

coming haploid. These males produce two kinds of sperm, functional and non-functional; there are just twice as many of the former as of the latter (Whitney). In this respect the case appears similar to that of the hornet, the male of which is haploid

and produces two functional sperm cells to one functionless. In the honey bee the situation is similar. The eggs usually give off two polar bodies thus becoming haploid. If such an egg is fertilized it produces a female (queen or worker), if un-

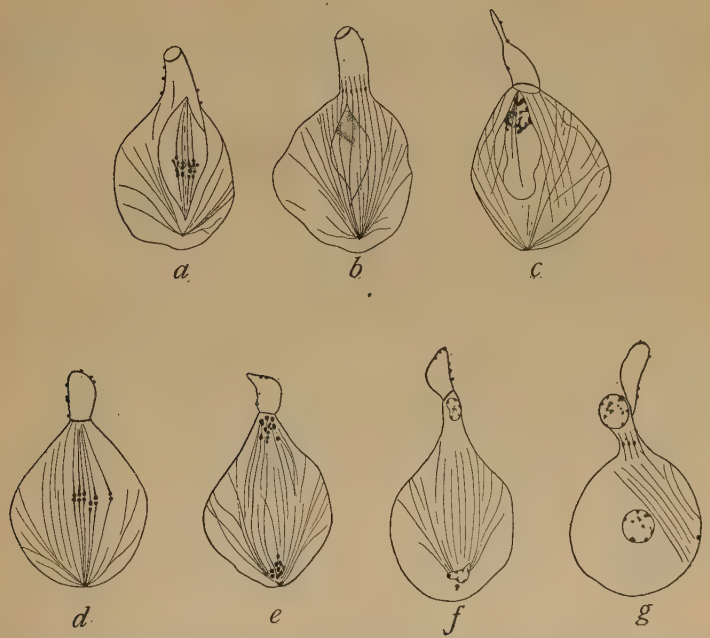


Fig. 33A.—Spermatogenesis in the honey bee. *a*, *b*, *c*, abortive first spermatocyte division. *d*, *e*, *f*, *g*, imperfect second spermatocyte division. (After Meves.)

fertilized it develops parthenogenetically into a male, which is thus haploid. In him the first spermatocyte division is abortive (Fig. 33, A, *a–c*), the second is more complete, two nucleated cells resulting, but one of them is very small and does not

develop further. Since one maturation division of the chromosomes, presumably equational, takes place, the functional sperm has the haploid number of chromosomes. All the sperm are alike, and any egg that is fertilized gives rise to a female, which is diploid.

In some of the aphids there may be a long succession of parthenogenetic females, whose continu-

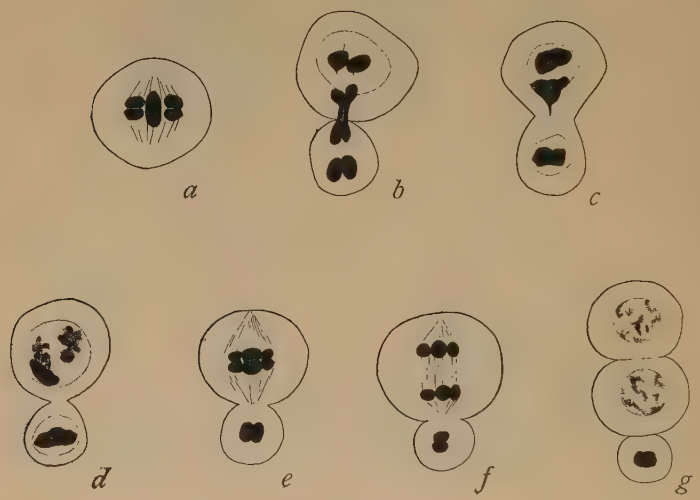


Fig. 33B.—Spermatogenesis of the bear-berry aphid. *a*, *b*, *c*, first spermatocyte division, with lagging chromosome. *d*, interkinesis stage. *e*, *f*, *g*, second spermatocyte division of functional cell.

ance has been shown to depend on environmental conditions. At the end of the series males and sexual females appear.

The parthenogenetic females have the diploid number of chromosomes (Stevens, von Baer,

Morgan). When the male appears, one chromosome less is found in his somatic cells, and, since in the nearly related phylloxerans a similar reduction takes place and has been seen (Morgan) to be due to the extrusion into the polar body of whole chromosomes, it is practically certain that in the aphids the loss takes place in the same way.

In the first spermatocyte division in the aphids (Fig. 33 B, *a–c*), one cell gets the unpaired X chromosome (the mate of the one lost in the polar body when the male egg matured), and this cell after another equational division (Fig. 33 B, *e–f*) produces two functional spermatozoa. The cell lacking the X degenerates. The sexual egg gives off two polar bodies. It then contains the reduced number of chromosomes including one X. Such an egg fertilized by the functional X-bearing sperm gives rise the following year to the stem-mother, which becomes the progenitor of a new line of parthenogenetic females, etc.

In the phylloxerans of the hickories the fertilized egg gives rise to a female called the stem-mother (Fig. 34). She emerges from the egg in the early spring and attaches herself by means of her proboscis to a leaf, causing it to produce a gall that envelops her. Within the gall she lays her eggs. These hatch, and produce the winged or migrant generation (Fig. 34). In one species, P. caryæcaulis, all the migrants in one gall are alike in that they produce the same kind of egg, *i.e.*, in some galls all the migrants contain large eggs (that produce sexual

females), while in other galls all of the migrants contain smaller eggs (that develop into males).

The sexual female lays one large egg, the winter egg, from which the stem-mother emerges the following spring. The males give rise only to female-

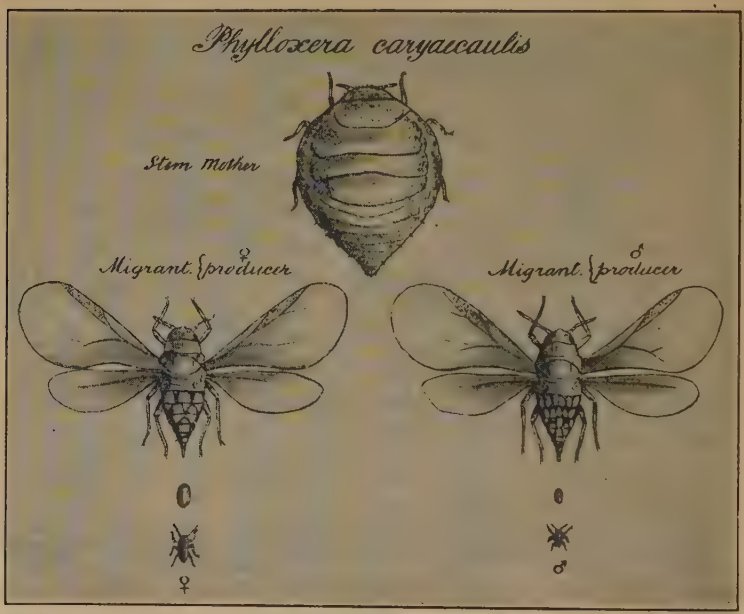


Fig. 34.—Diagram to illustrate the life cycle of Phylloxera caryæcaulis.

producing sperm, each spermatozoon containing two sex chromosomes. The other class of sperm degenerates. Hence we can understand why it is that all fertilized eggs produce females only.

The chromosomal cycle undergoes the series of changes shown in Fig. 35. In P. caryæcaulis there are eight chromosomes, including four sex chromo-

somes (XxXx). Since the history of the sex chromosomes alone furnishes certain information that makes clear some of the changes in the life cycle, the other chromosomes may be disregarded for the present.

Starting at the bottom of the diagram it will be seen that the sexual egg after extruding the two polar bodies contains two sex chromosomes indicated by X and x. Two kinds of males are indicated in the diagram, one containing Xx the other Xx′, and as a consequence there will be two kinds of female-producing sperm, one kind for each male, namely, Xx and Xx′. If the former fertilizes the sexual egg, the resulting stem-mother will be XxXx, if the latter, the stem-mother will be XxXx′. These two kinds of stem-mothers are indicated at the top of the diagram. One of them, XxXx, produces eggs which, after extruding one polar body, give rise to the migrants bearing large eggs; from the latter eggs, in turn, come the sexual females. The other stem-mother XxXx′, produces eggs, which, after extruding one polar body, give rise to the migrants bearing small eggs. Prior to the time when these small eggs are about to give off their single polar body, the two large X's conjugate and the two small x's conjugate, and when the polar body is given off one large and one small X pass out, and one large and one small X remain in the egg. In other words there is at this time a reduction in the number of sex chromosomes, and, as a consequence, a male is produced. Now, as the diagram shows,

Xx may remain in the egg and Xx′ pass out; or, in other eggs, Xx′ may remain in the egg and Xx may pass out. There will be, in consequence, two

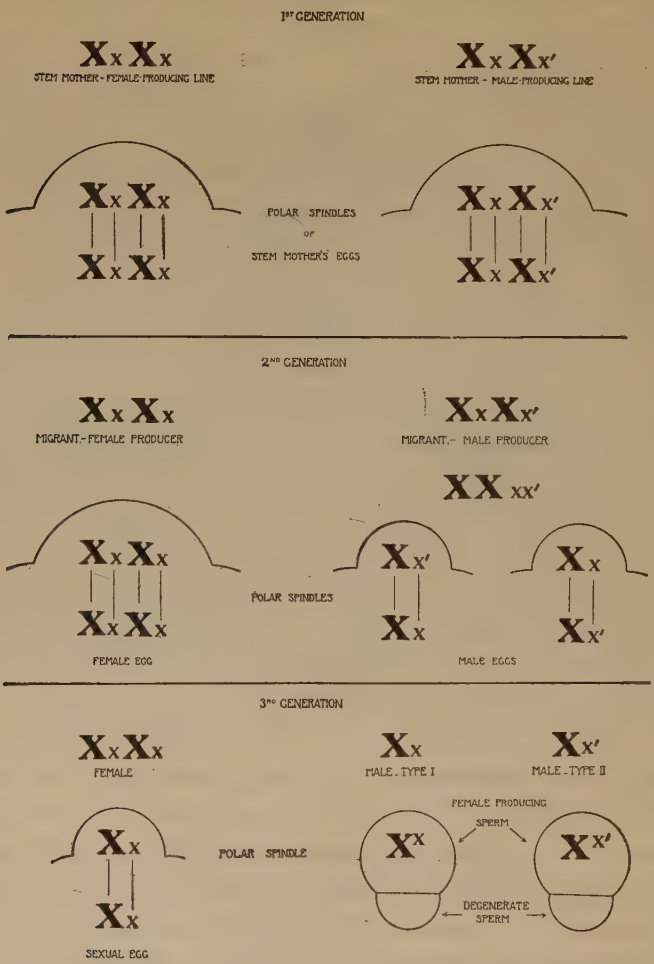


Fig. 35.—Diagram to illustrate the chromosomal cycle of Phylloxera caryæcaulis.

kinds of males, one Xx, the other Xx′, and as stated, two kinds of female-producing sperm Xx and Xx′.

Thus the life cycle is brought back to the starting point. It may be added that so far as the chromosomes other than the X chromosomes are concerned there is no synapsis and no reduction to the haploid number in either line until the maturation divisions of the third or sexual generation occur. The life cycle of this species illustrates three points:

First.—That all of the sperm are female-producing, because the male-producing class of sperm degenerates, as has been shown by direct observation.

Second.—That the parthenogenetic females can produce males through the elimination of two chromosomes. The female contains four sex chromosomes and the male two. The elimination of the two chromosomes in the polar body of the male-producing egg has been directly demonstrated.

Third.—In this species the somewhat unusual relation of one stem-mother giving rise to the line that culminates in the sexual eggs, and of another stem-mother giving rise to the line that culminates in the males, can be explained on the assumption that one pair of the sex chromosomes is heterozygous in some factor indicated in the diagram by priming one of the x's. This explanation is in part theoretical, although it is based on the actual observation of two kinds of males that differ in respect to the behavior of one of the smaller x's.

In other species of phylloxerans, and in many

aphids, one stem-mother may produce both lines; *i.e.*, some of her offspring may ultimately give rise to sexual females and others to males.

The Sex of Individuals Produced by Artificial Parthenogenesis

In only two species have individuals that have been produced by artificial fertilization been raised to a stage when their sex can be determined. Delage reared two such sea urchins, that were probably both males. Loeb has reared a number of frogs that were mostly males, but a few were females. Both sexes in Loeb's case appeared to have the diploid number of chromosomes; but until more is known of the chromosome situation in these cases it is not possible to offer any probable explanation of them. The work of Schmitt-Marcel and others also throws some doubt on the possibility of accurately determining the sex of frogs until long after metamorphosis.

Sex and Secondary Sexual Characters

Males differ from females not only in the gonads and in the accessory organs of reproduction (ducts, glands, copulatory organs) but often show more superficial differences that are called secondary sexual characters. Genes concerned in the differentiation of these have been shown, in two races at least, not to lie in the sex-chromosomes. These

characters are not sex-linked since they are not associated with a particular sex-chromosome, yet they may be said to be "sex-limited."

The first case is that of hen-feathering, shown by certain breeds of poultry. In Sebright bantams the males (Fig. 36, *a*) are hen-feathered. If either a male or a female Sebright is crossed to a race with normal cock-feathering the male offspring are hen-feathered. In the F_2 generation there are both

Fig. 36.—*a*, Normal Sebright hen-feathered cock. *b*, castrated Sebright cock.

cock-feathered and hen-feathered males. This shows that the dominant factors for hen-feathering are not in the sex-chromosomes, for, if they were, the F_2 generation from one cross would give only hen-feathered males, and from the reciprocal cross both kinds of males.

If a hen-feathered male is castrated the new feathers that come in—immediately if old feathers are plucked, otherwise at the next molt—are cock-feathered (Fig. 36, *b*). It is obvious that something

is produced in the testes of the hen-feathered birds, that, acting together with the somatic complex of the same bird, inhibits the full cock-feathering. It seems probable that an internal secretion is set free from the testes that acting in conjunction with substances produced in the feather follicles, causes the feathers to be like those of the hen, while in the absence of this secretion the follicles produce cock-feathering. In this case, one of the intermediate stages between the gene and the feather is located in the testes. It is interesting to note in this connection that when a hen has her ovary removed she also becomes cock-feathered (Goodale). In the ovary there are certain cells, called luteal cells, that are supposed to produce an internal secretion. In the adult of ordinary cocks these cells are absent, or rare, while in the testes of the Sebright, and also in the testes of another race of hen-feathered birds, the Campines, cells are present that look exactly like those of the female ovary. It seems plausible at least, that the secretion in question is produced by these cells and that it produces the same effect on the hen and on the hen-feathered male. In the Campines the hen-feathered males are recognized in some countries as the standard, while in other countries cock-feathered males are the standard. Here also it appears, although the evidence is less certain, that the two races differ by a factor for hen-feathering, and here too castration of the hen-feathered cockerel causes him to develop the cock-feathering like that of the other race.

In certain sheep, such as some races of Merinos (Fig. 36 A), the horns are present only in the ram. If a young ram is castrated his horns fail to grow. To study the inheritance of the factors involved in this difference it would be necessary to use for crossing with Merinos a different breed in which the horns were present (or absent) in both sexes, but such an experiment has not been made. There

Fig. 36A.—Merino sheep of Rambouillet. Ram horned, ewe hornless.

are other breeds of sheep in which both sexes are hornless (Suffolks), and still other breeds in which both sexes are horned, those of the ram being larger (Dorsets) (Fig. 36 B). The two latter have been crossed. It may be that we are dealing here either with factors for horns different from those in Merinos, or that modifying factors cause the different conditions. In this cross (Fig. 36 C) therefore it can not be said that we are studying

the inheritance of a secondary sexual character (for both sexes of the Suffolks are hornless and both sexes of the Dorsets are horned), but we are studying a single factor difference between the two breeds in question, a difference that is not sex-linked, but, is sex-limited in development. Horned Dorsets crossed to hornless Suffolks give horned sons and hornless daughters. If these are inbred they give three horned males to one hornless male, and three hornless females to one horned female.

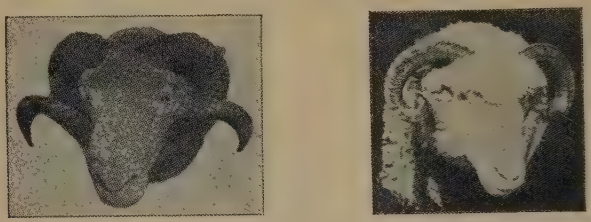


Fig. 36B.—Dorset sheep, both sexes horned, but ram with larger horns than ewe. (After Arkell.)

The results are explicable if a factor difference exists that is not in this case carried by the sex-chromosomes, and if in the male one gene for horns suffices to produce horns, while in the female two genes for horns are necessary to produce horns. For example, the horned breeds carry the genes HH, and the hornless breeds their allelomorphs hh. The F_1 sheep will be Hh♀ (hornless) and Hh♂ (horned). If the female is XX and the male XY, the F_1 gametes are as follows:

Gametes F_1♀ HX — hX

Gametes F_1♂ HX — hX — Hy — hY

Chance combination of any sperm with any egg gives eight classes in F_2 which are the eight classes described above. In this case the presence of

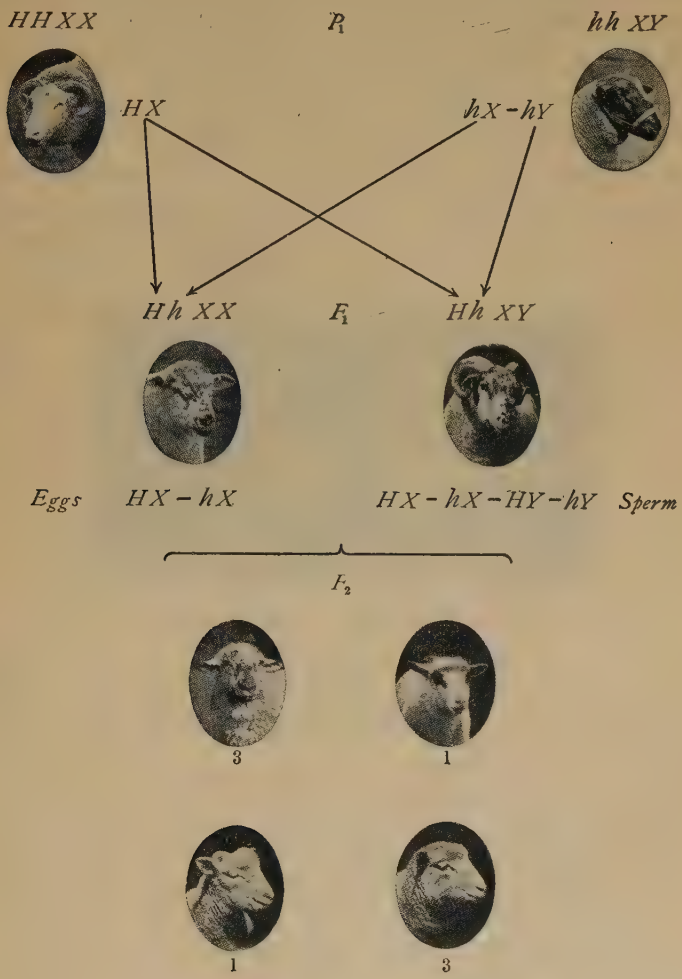


Fig. 36C.—Cross of horned to hornless race of sheep. (After Wood, photographs from Punnett.)

testes in the male is presumably the essential condition that brings about the development of horns in that sex when only one gene for horns is present. We have already seen that the castrated Merino ram fails to develop horns. In this case, then, some substance is produced by the testes that causes horns to develop. In another race, in which both sexes are horned, but the horns of the male are larger than those of the female, castration limits the development of the horns to the condition

Fig. 36D.—Euschistus. To left, E variolarius male; to right, E servus male. (After Foot and Strobell.)

shown by the females. In this race the testes cause the horns to develop to a higher stage than that shown by the female.

The second case is that of the two species of bugs (Fig. 36 *D*) viz. Euchistus variolarius and E. servus. The former has, in the male, a black spot on the ventral surface of the end of the abdomen, which is lacking in the male of the other species. Among the females of both species the spot is lacking. Foot and Strobell have shown that a

single factor difference distinguishes the two species in regard to the spot. The factor pair is not sex-linked, and is, therefore, autosomal. In other insects it has been shown by castration experiments that the development of the secondary sexual characters is not dependent on the presence of the gonad and if this relation holds also for Euchistus the factors must be supposed to produce their effects or not, according to the sex of the individual in which they occur.

Besides the above case of sex-limited characters in a wild species we have several cases among the mutant races of Drosophila melanogaster. These mutants are characterized by a greater effect of a gene on one sex than on the other, just as with the horns of certain races of sheep. Among mutants of this type are eosin, facet, and cut. Certain mutations produce a visible difference in only one sex; thus "side-abnormal" is distinguishable only in females, the males being entirely normal in appearance. A different type of this class is that in which the mutation affects some distinctly male or female organ such as "twisted penis," or "closed ovipositor." Certain mutant races also are entirely sterile in one sex but show a normal fertility in the other sex. Thus "cleft" and "giant" are male-sterile, while morula, fused and dwarf, are female-sterile.

In certain butterflies there are several types of females but only one kind of male. It has been shown by Punnett and others that such a state of affairs is explicable on Mendelian principles if we

assume that several genes are present that produce like effects in the male but different effects in the female, that is, the characters are sex-limited in development.

Parasitic Castration and Secondary Sexual Characters

It was first shown by Giard (1886) and later confirmed by Geoffrey Smith (1906) and others,

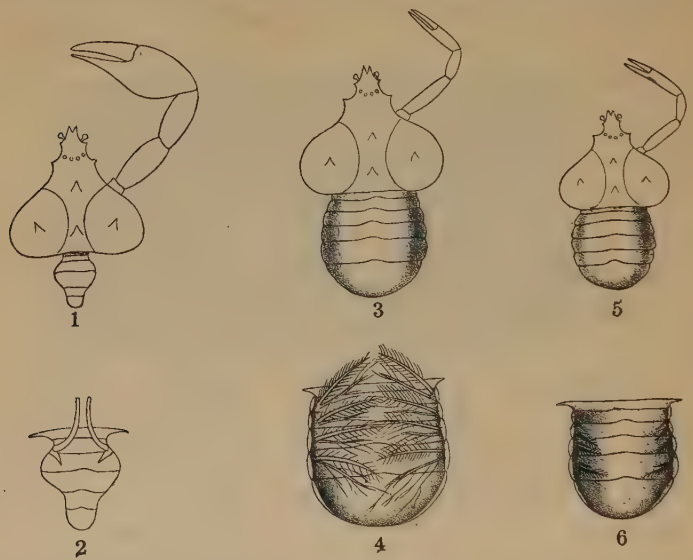


Fig. 36E.—1, 2, adult normal male; 3, 4, adult normal female; 5, 6, infected male that has assumed female characters. (After Geoffrey Smith.)

that when males (Fig. 36 *E*, 1–2) of certain crabs are parasitised by other crustaceans, such as Peltogaster, Sacculina, etc., they develop the secondary sexual characters of the female (Fig. 36 *E*, 5–6).

The testes are destroyed, as a rule, by the parasite, and this, no doubt, has given rise to the view that the changes in the secondary sexual characters are due to the removal of the testes—a view all the more plausible since such effects were well known in the mammals and birds. But Giard did not commit himself wholly to such a view. He appears to have thought that the influence of the parasite might equally well be due to direct action on the crab. The more general view, that the action is through the loss of the gonads, has been challenged by Geoffrey Smith. His view may appear to be the more probable interpretation, but as yet it has not sufficient experimental verification.

Kornhauser has recently discovered in one of the bugs (Fig. 36 *F*) a critical case that shows that a similar change in them is not due to the destruction of the gonad, but directly to some kind of influence on the tissues of the host. The nymphs of the tree-hopper Thelia bimaculata are parasitized by a hymenopter, Aphelopus theliæ. The egg deposited in the nymph produces a chain of young (polyembryony). The parasites in the male (Fig. 36, *F*, 1) cause it to develop certain characters, such as markings and some structural features, of the female (Fig. 36, *F*, 3–4). Usually the testes are destroyed; but in one case a testis was left and developed spermatozoa; nevertheless the nymph showed certain female characters. It is evident, therefore, that the change may take place independently of the gonads, and this is to be expected

in insects at least, where there is abundant experimental evidence (Oudemanns, Kopec, Kellogg, Meisenheimer, Regen) to show that there is no such relation as in mammals and birds.

Gynandromorphs and Sex

In species that normally have separate sexes individuals are occasionally met with that show

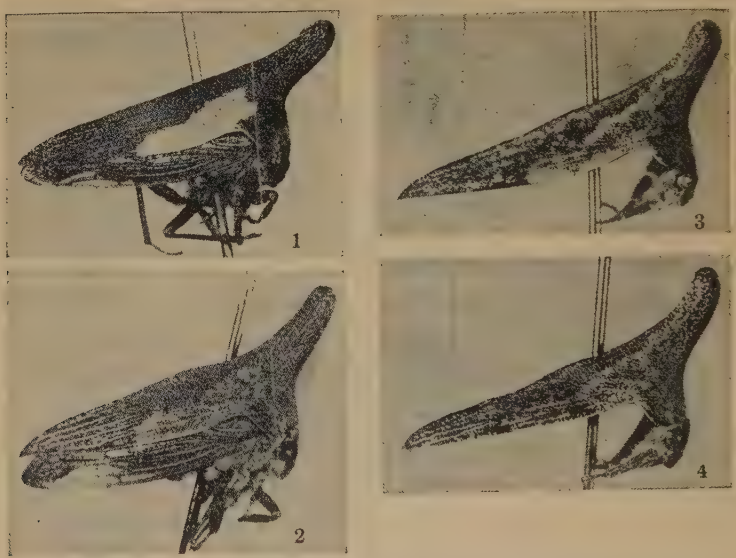


Fig. 36F.—Thelia bimaculata; 1, normal male; 2, normal female; 3 and 4, parasitized males. (After Kornhauser.)

male characters in certain parts of the body and female characters in other parts. All parts of the body may be involved, including secondary sexual characters, genitalia, and even the gonads. The

group of Lepidoptera has furnished more cases than all others taken together, although gynanders have been found also in bees, wasps, ants, and less frequently in other groups of insects; also they occur in spiders and lice, and rarely in crustacea and other groups of animals. It is seldom possible to discover the causes of these gynanders, either because their ancestry is unknown, or because the heredity of the characters involved has not been worked out. In Drosophila, on the other hand, over a hundred gynanders have arisen in pedigreed cultures, in which known hereditary characters were present; and, in fact, in some cases the cultures had been made up in such a way as to give critical evidence as to the origin of the individuals.

The most striking gynanders are those in which one side of the body is female and the other side male. The earliest of the completely bilateral gynanders found in Drosophila is that shown in c of Fig. 36 *G*. The right side of this fly was female throughout, and the left side male. The left side of head, thorax, and abdomen was smaller than the right side, the antenna, the bristles, the legs, and the wing of the left side were also smaller than the same organs on the right side. Besides these differences in size, the left fore-leg bore a distinctly male character, the sex-comb, and the left side of the abdomen was colored and segmented as in the male. The genitalia (in *c*, of Fig. 36, *G*) were distinctly of the male type on the left side, but on the right the structures are neither purely female

nor male. Ovaries were present in both sides of the abdomen. The like character of the two gonads is possibly due to the development of both from a single cell set aside early in development.

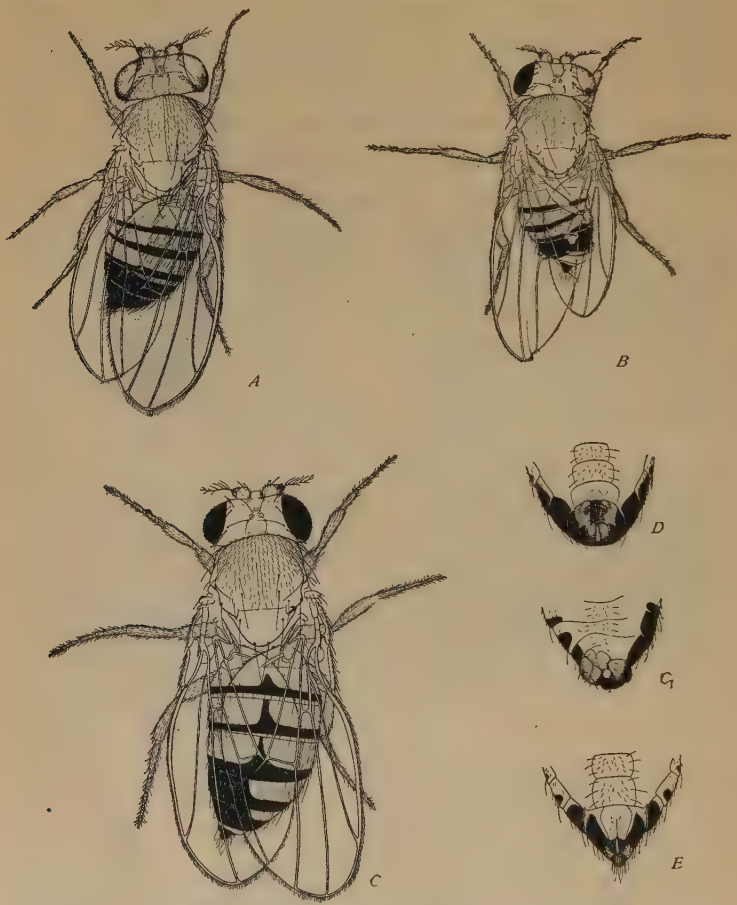


Fig. 36G.—*A*, *B*, *C*, three gynanders of Drosophila, male on one side, female on the other. *C*, genitalia of gynander *C*; *B*, of normal male; *E*, of normal female.

In another case (*A* of Fig. 36 *G*) sex-linked characters were present that appeared in the gynander. In this gynander the left side of the thorax and abdomen was male, but the head was entirely female. The male parts all showed the usual sex differences, and also the sex-linked recessive character yellow body-color (unstippled). This gynander arose from an egg, carrying an eosin-bearing X, fertilized by an X-sperm bearing

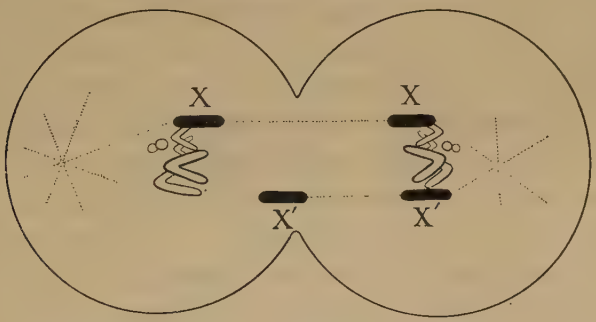


Fig. 36H.—Diagram illustrating elimination of one sex-chromosome.

the genes for yellow and white. The zygote was therefore female, and the female parts of the gynander retain the above constitution. If at the first segmentation division, the paternal (yellow white) X divided normally and each daughter nucleus received a yellow white X, but one daughter chromosome of the other or maternal (eosin) X failed to pass to the pole with the other chromosomes (Fig. 36 *H*), then one of the two nuclei that resulted from such a division was XX in constitution

and gave rise to the female parts of the gynander, while the other nucleus carried only the yellow white X and gave rise to the male parts of the gynander.

Another gynander, shown in *B*, Fig. 36 *G*, started as an XX zygote that received the three characters cherry (recessive) abnormal-abdomen (dominant) and forked (recessive) from the mother, and vermilion (recessive) from the father. The female parts show the dominant abnormal-abdomen. There was elimination of a daughter vermilion X-chromosome at the first, perhaps at the second nuclear division, so that the male parts show all three maternal characters cherry abnormal and forked. Both fore-legs were male (sex-combs and forked bristles); the right side of the thorax was male (smaller size, smaller bristles and hairs, forked bristles, smaller wing); the right side of the head was male (cherry eye-color, forked bristles, etc.), except for a tiny island of female tissue, red in color, in the rear margin of the eye. The abdomen was male on the right side as shown by the smaller size, the more extreme abnormality, and somewhat by the coloration.

In other gynandromorphs the anterior parts may be female and the posterior male, or vice versa. Only one quadrant may be male and the rest female, or even smaller portions may be male, according to whether elimination occurs at an early or a later cleavage. Islands and streaks of one sex and the irregular dividing line sometimes seen in the head

or abdominal region may be due to the shifting of nuclei in embryonic development.

Previous explanations of gynanders have involved the use of whole nuclei, and have postulated that the male parts are haploid, and the female parts diploid. The gynanders of Drosophila have been explained by the behavior of an intra-nuclear element—the X chromosome—and the cells of both sexes remain diploid for the autosomes. That both maternal and paternal autosomes were present in both male and female parts of the Drosophila gynanders was decisively proved in certain cases by the introduction of autosomal characters as well as sex-linked characters. In the gynanders that arose in such crosses both sex-regions showed the same condition with respect to these autosomal characters.

There are a few gynanders in Drosophila that can not be explained by simple elimination; but another explanation appears to cover such cases, namely that two nuclei were present in the egg before fertilization. If one of these nuclei was fertilized by an X-sperm and the other by a Y-sperm the two halves of the resulting embryo may be of different sexes, and even display different sex-linked characters according to the constitution of the two nuclei. The two interesting gynanders described by Toyama in the silk-worm moth (Fig. 36 *I*) call for this type of explanation (Fig. 36 *J*). In this connection it is interesting to note that Doncaster has found binucleated eggs

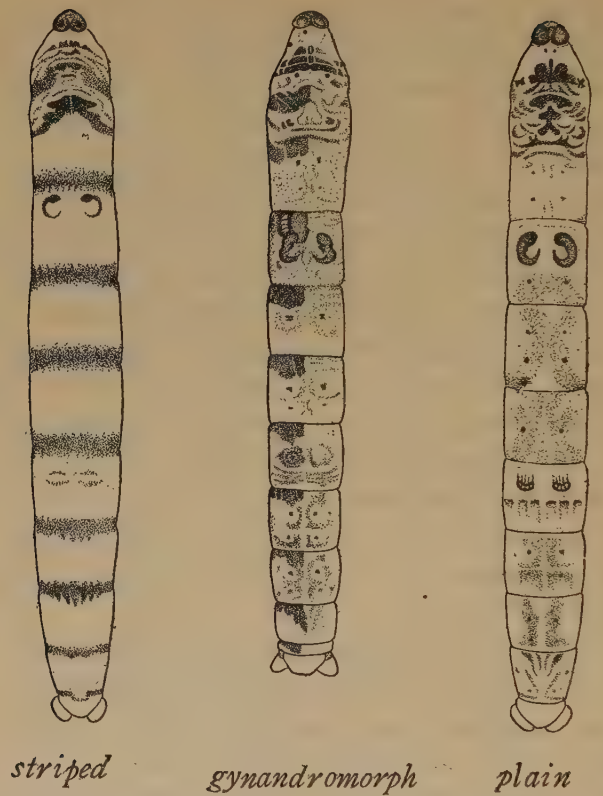


Fig. 361.—Caterpillars of silkworm moth. The gynandromorph is a hybrid between the striped and plain races. (After Toyama.)

in the moth Abraxas, and has observed that each nucleus is fertilized by a single spermatozoon.

In the famous Eugster hive of bees studied by von Sieboldt large numbers of gynanders were found. A similar case is recorded by Engelhardt, and more recent cases by Sheppard. The explanation of these cases is less certain than those

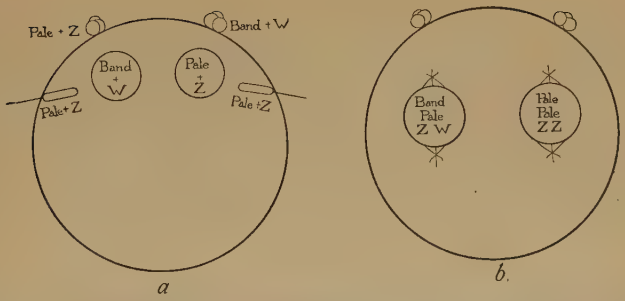


Fig. 36.J—Diagram giving the explanation of the gynander in Fig. 36.I by means of a binucleated egg.

of the flies. One possible explanation has been suggested by Boveri, namely, that a sperm enters an egg that has already begun its first division and fuses with only one of the resulting nuclei from the first division (Fig. 36 *K*, *A*). This double nucleus should produce female parts, while the single

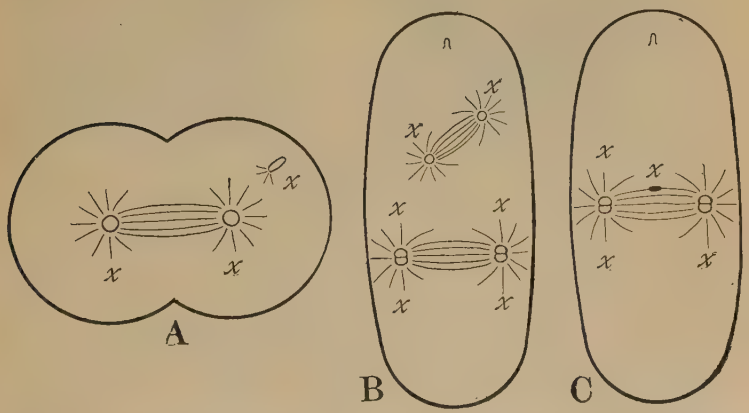


Fig. 36K.—Diagram illustrating three theories of gynandromorphism *A*, Boveri's theory of partial fertilization; Morgan's theory of supernumerary sperm; *C*, theory of elimination, as in 36H

nucleus should give rise to male parts. Another suggestion was made by Morgan, namely that one sperm fuses with the egg nucleus and gives rise to female parts, while another sperm that has also entered, develops independently and produces male parts (Fig. 36 *K*, *B*). It is known that more than one sperm may enter the egg of the bee. A third explanation is offered by the theory of elimination of a daughter X-chromosome (Fig. 36 *K*, *C*), as in Drosophila. This explanation would apply in those cases where the bees were hybrids, provided the racial characters that were involved in the Eugster bees and in von Engelhardt's bees are carried by the sex-chromosome—a point not yet determined.

Intersexes and Sex

As first shown by Brake, remarkable mosaics of male and female characters are found in hybrids between the European and Japanese varieties of gipsy moths *Porthetria dispar* and *japonica*, when the cross is made one way but not when made the other way. We owe to Goldschmidt not only a most complete account of such hybrids but also of hybrids between several Japanese local varieties of this moth. A most astonishing series of mixtures of male and female characters come to light, not as sporadic occurrences, but as regular phenomena of the crosses. In his earlier work Goldschmidt called these mixed forms gynandromorphs, but his

later work shows, he thinks, that they are different from gynandromorphs; he now calls them intersexes.

The normal males and females of the gipsy moth differ not only in the characteristic sex differences of this group, but in other secondary sexual differences also (Fig. 36 *L*). The Japanese varieties show these same differences. *Japonica* female by

Fig. 36L.—Gypsy moths. *A*, normal male, *B*, normal female. *C*, *D*, "intersexes." (After Goldschmidt.)

dispar male gives equal numbers of daughters and sons, which are normal as to sex; but the reciprocal cross, *dispar* female by *japonica* male gives normal males and intersex or male-like females in equal numbers.

The intersex females from the last and from other crosses show a wide range in structure, in color,

and in behavior, varying from almost normal females at one end of the series to forms that externally are about like the normal male. Not only are the wings in extreme cases colored like those of the normal male (with, however, occasional flecks of white like the female), but the size and diverse parts such as the antennæ, the hair, the genitalia, and even the gonads are mosaics of male and female characteristics.

These relations are more interesting when crosses involving different Japanese races are compared. When Jap. G. male is crossed to Jap. K. female, all F_1 daughters are *slightly* intersexual or male-like. When Jap. H. female is crossed to Jap. G. male, the daughters are somewhat more like males, but their instincts are female, and they attract males. The copulatory organs are so changed in the direction of the male that mating is unsuccessful; and eggs can not be laid, although characteristic hairy sponges are made to receive them. When Eur. F. female is mated to Jap. G. male, the daughters are more than half-way transformed into males. The secondary sexual characters are almost male. The instincts and behavior are about intermediate between those of the male and female of the two normal races. Males are scarcely, or not at all attracted, and no mating occurs. The copulatory organs show the strangest combination of male and female types. There are still typical though rudimentary ovaries. When Jap. X female is crossed to Eur. F. male, a still higher degree of

intersexuality appears. Externally the daughters are "almost indistinguishable from normal males." The instincts are entirely male and the moths try unsuccessfully to mate with females. The gonads look like testes, but show in sections a mixture of ovarian and testicular tissue. A step further and the daughters would be completely transformed into males. The next cross gives this final stage. When Jap. O male is crossed to any race of European female, only males are produced, *i.e.*, all the daughters become sons.

The reverse picture is given by those combinations in which the intersexes are sons partly changed over into daughters, a condition that Goldschmidt terms male intersexuality. The wings are generally streaked with white and in the extremest type only a few spots of the brown characteristic of the male appear on the wing-veins. The testis may contain some ovarian tissue, but the changes in the gonads do not appear to run parallel to those seen on the surface.

The explanation that Goldschmidt offers for these intersexes is entirely different from the explanation that is demonstrated for the gynandromorphs of *Drosophila*. He accepts the chromosome theory of sex determination, and applies it to the present case on the basis that the female is heterozygous for the sex chromosome Mm (ZW), and the male hymozygous MM (ZZ). In addition, however, Goldschmidt adds another set of sex-determining factors that he calls FF (inclosing them in brackets),

which he locates either in the cytoplasm, that is, outside the chromosomal mechanism, or, more probably, in the W chromosome. These factors do not segregate, and are transmitted from the female to her sons and daughters alike. The FF factors stand for femaleness, which apparently includes the eggs, ovaries, secondary sexual characters, and genitalia, in fact, all parts associated with the female. The sex of a given individual is dependent on the balance struck by the activity of the factors Mm and FF.

One illustration of the kind of explanation advanced by Goldschmidt may be given. As stated, he represents the female by FFMm, and the male by FFMM. If in a certain race the FF "factorial set" is represented by 80 units, and the "present" male factor, M, by 60 units, then the above formula for the female becomes $80 - 60 = +20$, and the male formula becomes $80 - (60 + 60) = -40$. In the former, female units "dominate," in the latter, the male. Values like these can be arbitrarily set for all the different races. For instance the following values are assigned to the "weak" European race and the "strong" Japanese:

Weak European Race			Strong Japanese Race		
♀	(FF)	Mm	♀	(FF)	Mm
	80	60		100	80
♂	(FF)	MM	♂	(FF)	M M
	80	60, 60		100	80, 80

If a Japanese female is crossed to a European male, the F_1 female and male may be represented in the following formula:

F_1 ♀	(FF)	Mm	F_1 ♂	(FF)	M	M
	100	60		100	80,	60

Both "normal" female and male offspring are expected in equal numbers. The reciprocal cross gives a different result viz.:

F_1 ♀	(FF)	Mm	F_1 ♂	(FF)	M	M
	80	80		80	80,	60

The F_1 female is FF – M = 0; and is therefore represented as intersexual. It will be observed that the so-called "female factors" in these formulæ are supposed to be inherited entirely through the mother.

By assigning different values to FF and M in the different races it is possible to express the results in such a way that the sexes obtained by various crosses have different minimal values—those less or more than any assigned value for a given sex are interpreted as intersexes. In the example cited, an exact balance (= 0) between the conflicting factors produces an individual that is neither male nor female, but made up of a mosaic of parts each of which is roughly comparable to the same part in a male or a female.

A series of crosses between species of Biston have been made by J. W. Harrison. The sex ratios are altered and in some cases intersexual females

appeared. The results are in many respects like those of Goldschmidt.

Sturtevant has studied a race of intersexes in Drosophila simulans. The intersexual individuals are all alike, and have parts that are characteristic of normal individuals of both sexes (ovipositor, seminal receptacle, etc., of female; genital segment, claspers, anal plates, etc., of male). Genetic evidence shows that the intersexes are females, in that they have two X-chromosomes, even in the male-appearing parts. The result is produced by a second-chromosome recessive mutant gene. In this case, then, we are dealing with a modification of the development of the female,—not with a disturbance in the usual sex-determining mechanism. In the cases of intersexuality recorded by Goldschmidt, Harrison, and others there seems to be no proof that there is a single sex-determining gene that has a different "potency" in different species. The case of Drosophila simulans shows that it is not admissible to assume such an explanation without proof.

Triploid Intersexes in Drosophila Melanogaster

In *Drosophila melanogaster*, Bridges has found a strain that continually produces individuals that are intermediates between males and females. These "intersexes" can always be easily distinguished from normal males or females because of their larger size, their coarse-textured eyes, and by other

characters peculiar to them. Within the class, there is great fluctuation—on the one hand to individuals entirely male in appearance, and on the other to individuals nearly all of whose characteristics are female. An intersex of a high "female-type" is an individual in which most of the parts are purely female, a few parts are male, and others are mixtures. The mid-grade intersexes usually have rudimentary ovaries; but not infrequently one gonad is a rudimentary testis, or a rudimentary ovary with a follicle budding into a testis. The testes of high grade male-type intersexes are like those of normal males in size and appearance. All intersexes are sterile. The stock is maintained by breeding from sisters of the intersexes. Only a small proportion of these gives intersexes. Genetic tests and cytological examination show that the intersex-producing females are triploid (3n), possessing three representatives of each of the four chromosomes. Likewise the intersexes are shown to be triploid for the autosomes, but only diploid for the X-chromosomes. Individuals with two X-chromosomes are not females if a third set of autosomes is present; they are altered to a greater or less extent into males. Accordingly, the autosomes are shown to be as concerned in the production of sex as are the so-called sex-chromosomes. The X-chromosomes are seen to be chromosomes that are female determining in tendency, while the autosomes are male determining.

If the chromosomes determine sex by means of

genes carried in them, we may say:—both sexes are due to the simultaneous action of two sets of genes, one set, located predominantly in the X-chromosome, tending to produce the characters called female, the other set, located predominantly in the autosomes, tending to produce the characters called male. These two sets of genes are not equally effective, for the female-tendency genes outweigh the male-tendency genes, and the diploid (or triploid) form is a female. When the relative number of the female-tendency genes is lowered by the absence of one X, the male tendency genes outweigh the female, and the result is the normal haplo-X male. When the two sets of genes are acting in a ratio between these two extremes, as is the case in the ratios of *2X : 3 sets of autosomes*, the result is a sex intermediate—the intersex.

Individuals that have *3X: 2 sets of autosomes* (superfemales) and *1X : 3 sets of autosomes* (supermales) are likewise produced by triploid (3n) females. They have been identified by genetic and cytological tests. They form distinct types that are easily distinguishable from normal females or males, and they are sterile.

Sex and Sex-determining Gametes

The word sex is usually applied to many-celled individuals, the male sex producing sperm and the female sex producing eggs. In most races the male and the female sex have the diploid (double) number

of chromosomes; in some races the male has one less chromosome than the female, in other races the female has one less than the male. There are races in which the male has the haploid (full) number of chromosomes, while the female has the double number. The gametes giving rise to these two kinds of individuals are sometimes loosely referred to as male and female, but they are properly only male-producing and female-producing in certain *combinations;* for, as shown in non-disjunction, the same gametes if they form other combinations may give a result that is just the opposite from that which usually occurs. Thus, a "female-producing" X-sperm will give rise to a male if it enters an egg without an X.

The same terms male and female have been carried over to the protozoa—organisms that are one-celled like the gametes of multicellular forms; but obviously the words are here used in a different sense. In what manner the protozoa are to be compared with the higher forms remains uncertain until we have more definite information concerning the chromatin changes that take place before, during, and after, conjugation.

In the mosses and liverworts an interesting situation exists. There are two alternating generations, one is diploid (sporophyte), the other haploid (gametophyte). In mosses and liverworts with separate sexes the sexual generation is haploid.

Allen has found in one of the liverworts, Sphærocarpus, that there is an unequal pair of chromosomes

in the cells of the sporophyte generation (diploid). In the female gametophyte (haploid) the larger member of the pair is present, and in the male gametophyte (haploid) its smaller mate. At the reduction division in the sporophyte, when four spores are formed, two of the spores in each tetrad contain each a large chromosome and two a small one. It is fairly well determined that from each set of four spores, two give rise to female plants of the gametophyte generation, and two to male plants. In this case the males and females are plants with the haploid number of chromosomes, one with the large chromosome and the other with the small one. The sporophyte being diploid contains both chromosomes, which, as stated, are separated again when the spores are formed, *i.e.*, at a time corresponding, it would seem, to the maturation division of the egg and the sperm.

It may be recalled in this connection that the male bee and the male Hydatina are haploid organisms; but in them, unlike the haploid gametophyte generation of the liverworts and mosses, modified maturation divisions occur. By means of alterations in the maturation divisions female-producing gametes only are produced.

Sex-ratios

Both the XX–XY and the WZ–ZZ types give equal numbers of males and females, provided that both kinds of gametes are equally viable, that

random fertilization occurs, and that the resulting zygotes are equally viable. There is evidence bearing on all these possible sources of disturbances of the normal sex-ratios.

In the males of aphids and phylloxerans all of the no-X gametes degenerate; in the male bee three of the four gametes fail to develop; in the hornet two of the four; in Hydatina one of the primary spermatocytes gives rise to two female-producing gametes, the other, which would give rise to male-producing gametes, fails to divide and then degenerates. In all of these cases fertilization produces only females. The imperfect pollen grains that are found in many plants, do not appear to come under this heading, since they are not involved in sex-determination.

Much of the genetic work goes to show that selective fertilization does not take place. There is one set of direct observations, on the unisexual mollusk, Cumingia, that shows that the first sperm that meets the egg, head on, enters the egg and fertilizes it. It has been suggested that under environmental conditions unfavorable to the spermatozoa, one kind may be affected more seriously, or sooner, than the other kind, and thus bring about a selective result; but no direct evidence has ever been brought forward to substantiate such a view. That one class of spermatozoa may travel faster and hence may more often succeed in reaching the egg first is a suggestion that is perhaps less hypothetical than the last. Zeleny and Faust's careful

measurements of the sperm of insects, especially those in which the female- and male-producing sperm differ by a large X-chromosome, and the later results of Goodrich in Ascaris incurva show that the two classes of sperm may differ in size to a considerable degree. (Fig. 36 M).

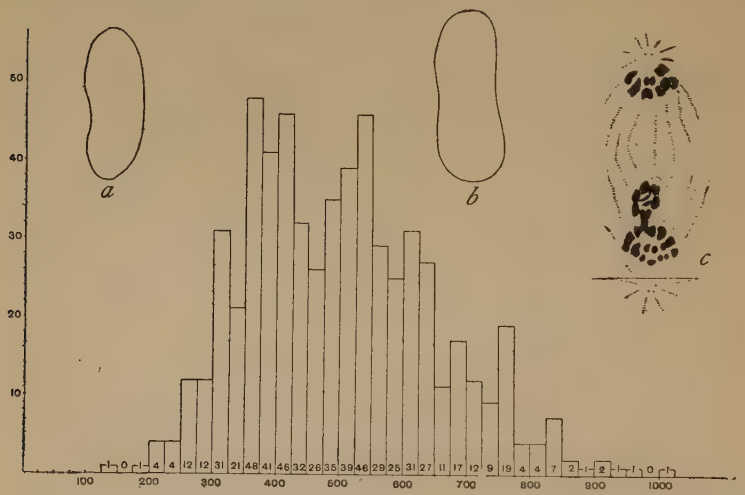


Fig. 36M.—Curve showing dimorphism of sperm of Ascaris incurva. *a*, outline of nucleus of one class, *b*, of other class of sperm. *c*, telophase of differentiating division. (After Goodrich.)

During the long passage up the oviduct of a mammal, it is possible that the lighter male-producing sperm may travel faster than the female-producing sperm and therefore attain the upper reaches of the oviduct in larger numbers. More males than females would then be expected, and it is noteworthy that this is the case in several mammals, including man. Correns has obtained evidence that

in Lychnis the male-producing pollen do not fertilize proportionately as many eggs in competition as they do when not enough pollen is present to fertilize all the eggs. Presumably the pollen-tubes do not grow as fast as those of the female-producing pollen.

There is one situation that calls for special notice. In the WZ—ZZ type (moths and birds) the egg contains WZ in conjugation before the polar bodies are extruded. If it is only a matter of chance which way this pair (WZ) lies on the spindle, then equal numbers of W-eggs and Z-eggs result after the polar bodies have been given off. But if the WZ pair should be placed so that the Z went out more often, more females would be expected; and if the W went out more often, then more males would result. Now in a few cases (Doncaster and Seiler) the W-chromosome is absent. In the egg of such a female there would be a "lagging" Z on the maturation spindle and if this tended to pass out (or to be lost) more often than to remain in the egg, the sex-ratio would be turned toward females. In fact any sex-ratio might result from the OZ type of individual. Moreover, once started, such an OZ line would perpetuate itself. In the case of the Y chromosome of the XX—XY type it makes no difference in the sex-ratio to which pole the X goes since both poles produce functional sperm, and the Y has disappeared in many cases.

Another way in which sex-ratios are influenced is through the viability of the zygotes. In extreme cases, occurring in Drosophila all the offspring of a

female may be daughters. Sex-linked lethals cause this. A sex-linked lethal is inherited in the same way as any other sex-linked gene, but causes the death of any male that carries the gene in his single X chromosome. A female, heterozygous for such a recessive lethal, will survive. She produces only half as many sons as daughters. Such 2 : 1 ratio strains can be continued indefinitely by simple breeding methods. A female may even be heterozygous for two different recessive lethals. If these lethals are both carried in the same member of the X-pair, and are close together in the chromosome, only a few more than half the sons will be eliminated; but if they are far apart, so that crossing over between them is frequent, as many as three-fourths of the sons may be killed. If the two lethals are in opposite members of the X-pair and far apart, then also about three-fourths of the sons are eliminated; but the closer together the loci of these opposed lethals are, the greater is the proportion of sons killed. Thus, two sex-linked lethals may determine any sex-ratio from 2♀ : 1♂ to 2♀ : 0♂, according to the particular linkage relations. There is also a large class of sex-linked mutations in Drosophila that are "semi-lethal." Some of them kill all males except an occasional one, while still others allow more males to come through, the numbers of male survivals being characteristic for each type, and ranging up to the normal 1 : 1 ratio.

Lethals that kill female zygotes are not as common as lethals that kill males. There are two

sex-linked and two or three autosomal mutants that are semi-lethal to different degrees in the female but kill fewer males. One of these sex-limited semi-lethals gives only male families under certain environmental conditions.

The sex-ratio in the honey bee has no fixed value. At one time of the year all of the offspring may be daughters (queens and workers), and at another time many sons may be produced. If the sperm supply of the queen gives out, or if the queen has not been fertilized, all of her offspring will be males. The sex-ratio varies therefore from 100: 0 to 0: 100. The determining factor for sex is two-fold, an internal one producing only X-spermatozoa (that accounts for the females) and an environmental factor, namely, the conditions that determine whether an egg is or is not fertilized. If it is not fertilized, it produces a male by parthenogenetic development.

Worker bees that are modified females may on rare occasions lay eggs that develop parthenogenetically. Such eggs produce males. While this is the rule for most of the domesticated races of bees, there has recently been described a race of African bees whose workers readily produce offspring of both sexes. In ants also there are well authenticated cases where both queens and males have been produced in queenless nests, although as a rule sex in ants is determined as in bees, *i.e.*, only males arise from unfertilized eggs. It seems not improbable in these exceptional cases that one of the

reduction divisions is supressed when a worker's egg gives rise to a female. Such a supposition finds some support in the fact that in other groups of Hymenoptera (saw flies and gall flies) females arise regularly from unfertilized eggs. In some of the species of gall flies, males are unknown; in others they appear very rarely.

The female of Dinophilus apatris produces large and small eggs in equal numbers. From the former arise females, from the latter males (Korschelt, von Malsen, Shearer, Nachtsheim). The small eggs may predominate in some of the earlier laid batches, so that at this time sons are in excess, but if the mother remains alive, so that the full output is produced, the sex-ratio becomes 1 to 1 (Nachtsheim). If the mother dies early, there may appear an excess of males. What factor determines whether an egg is to become a large female-producing egg, or a small male-producing egg is not known. The suggestion, that the difference in size is due to the number of yolk-bearing cells that are absorbed by the egg during its growth period, has been disproven by Nachtsheim; for he finds at the end of that period that all the eggs are of the same size and the difference in their size comes in later.

CHAPTER V

THE CHROMOSOMES AS BEARERS OF HEREDITARY MATERIAL

The evidence in favor of the view that the chromosomes are the bearers of hereditary factors comes from several sources and has continually grown stronger, while a number of alleged facts, that seemed opposed to this evidence, have either been disproven, or else their value has been seriously questioned. We propose now to examine in some detail the observations and experiments that bear on the chromosome theory of heredity.

The Evidence from Embryology

Relating to the Influence of the Chromosomes on Development

It has been argued that since the sperm transmits equally with the egg, and since only the sperm head, consisting of the nucleus, enters the egg, inheritance is only through the nucleus. But it must be admitted that around the entering sperm nucleus there may be a thin enveloping protoplasm, which, however scanty, might suffice to transmit certain cytoplasmic factors. Moreover, while the tail of the sperm appears in some cases to be left outside the

egg, in other cases it appears to enter and to be absorbed.

Behind the head of the spermatozoon, and at the base of the tail, there is a middle piece which contains a derivative of the old centriole or division center. Since the centrosome carried by the sperm has been found in some forms to give rise to the new centrosomes that occupy the poles of the first cleavage spindle of the egg, it may appear that a paternal contribution can come about in this way. It is true that the continuity of the centrosome of the sperm with that of the dividing egg has been disputed in some forms; but it is difficult to prove that the sperm centrosome is lost, even though it may disappear owing to loss of staining power.

The nucleus contains a sap which is probably of cytoplasmic origin. The presence of this sap may again be appealed to by those who do not accept the chromosomes as the bearers of heredity, as a weak link in the evidence. It is true that the nuclear sap appears to be squeezed out of the nucleus of the sperm head, leaving a compact and apparently solid mass of chromatin, yet its complete elimination can not be proved. Hence, while those who favor chromosomal transmission find in the facts of normal fertilization strong *indications* favorable to that view, yet it is also true that those who are inclined to dispute this view find several loopholes in the argument of their opponents.

The importance of the nucleus in heredity has further been shown by experiments of Bierens de

Haans, Herbst, and Boveri on giant eggs of sea urchins fertilized by sperm of another species. The hybrid larvæ produced when normal eggs of one species are fertilized by sperm of the other species are intermediate in character between the two parental types of larvæ; while those from giant eggs of the same species fertilized by sperm of the other, also intermediate, incline more to the maternal side. The nucleus of the giant egg is double the size of that of the normal egg and according to Bierens de Haans the chromosomes are also double in number. Consequently, the amount of maternal chromatin should be double that introduced by the sperm, and might produce a corresponding influence on the hybrid character. But since in these giant eggs the cytoplasm is also doubled, it is not evident that the results are due to the chromosomes rather than to the cytoplasm. By means of the following ingenious comparison Boveri has shown that the results must be ascribed to the chromosomes rather than to cytoplasm. Normal eggs were broken into fragments, the nucleated pieces were fertilized with the sperm of the other species, and those fragments of half the volume of the normal egg were isolated. As is known, such fragments develop into whole larvæ, whose nuclei will have the usual chromatin content. The egg cytoplasm is, however, reduced to half. Nevertheless the larvæ did not incline to the paternal side, although these larvæ, like all larvæ from fragments, were often simpler than the normal. Hence since a relative decrease in the amount of

cytoplasm does not here affect the character of the larvæ, it is rational to suppose that an increase such as is present in the giant eggs likewise produces no such effects as observed in the larvæ. At the same time, normal eggs were cross fertilized and in the two-cell stage the blastomeres were separated. The contributions by the two parents were relatively the same as in the normal egg. These larvæ were like those from egg fragments, and serve as a control of those larvæ in so far as they bear on the question of how far size alone may affect the result. Moreover, in them, the relation of the chromosomes to the cytoplasm is the same as in the normal egg (whether the sperm does or does not bring in cytoplasm). Hence, since the amount of cytoplasm is shown to have no influence on the character of these larvæ, there is no reason for supposing that it had any influence in the case of the giant eggs.

Boveri's studies upon dispermic fertilization of the egg of the sea urchin bear directly upon the question at issue. He found that when two sperm simultaneously enter the same egg, each brings in a centrosome, so that a tetra- or tri-polar spindle is formed for the first division, as shown in Fig. 37. Instead of a double set of chromosomes, as in normal fertilization, there are three sets. At the first division, the chromosomes are irregularly distributed upon the multipolar spindles. In consequence, some cells may get one of each kind of chromosome, while other cells may get less than a full complement (Fig. 38). These dispermic eggs almost always give

rise to abnormal embryos, as several observers have recorded. The result can best be attributed to the irregular distribution of qualitatively different chromosomes; only those embryos in which each cell has a full complement developing normally.

Boveri's evidence went still further, for he separated the first cleavage cells of these dispermic eggs

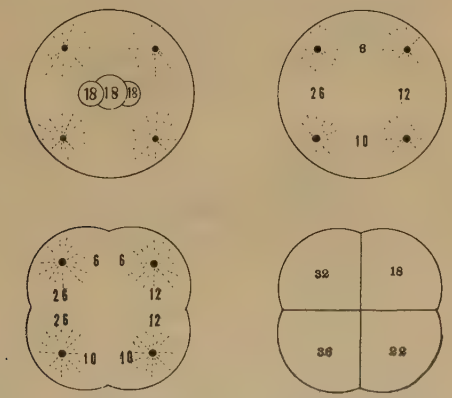


Fig. 37.—Dispermic fertilization of egg of sea urchin. The four centrosomes cause an unequal distribution of the fifty four chromosomes, leading at the first division to four cells which contain different numbers of chromosomes.

and followed their history. Some of them gave rise to perfect dwarf larvæ. The number of normal embryos was small, but was that expected on the chance distribution of the chromosomes, for we should expect to find in a few cases an isolated cell that contained a full complement of chromosomes and from such a cell a normal embryo would be formed. The abnormality in development of the rest of the isolated cells was not due to any harmful

effect caused by isolation, for it had been shown by Driesch and others that when the first two cells of a sea-urchin egg that has been normally fertilized are separated, each forms a perfect embryo. Such cells, although containing only half the cytoplasm, contain

FIG. 38.—Diagram to show five combinations of chromosomes resulting from the first division of dispermic eggs, in which either each cell gets one complete set of chromosomes, *a*; or three cells get a full set, *b*; or two cells, *c*; or one cell, *d*; or none of the four cells, *e*, get a full set. (After Boveri.)

a full set of chromosomes. The difference, therefore, between these cells and isolated cells from dispermic eggs would seem to be due mainly to their different chromosomal contents.

Further evidence in favor of the chromosomal hypothesis is found in certain cases of hybrids between

species of sea urchins. The best analyzed cases are those that Baltzer has worked out. Crosses were made between four species of sea urchins; one such cross will serve as an example (Fig. 39). The eggs of Sphærechinus were fertilized by the sperm of Strongylocentrotus. The division of the chromosomes proceeded in normal manner. The pluteus

FIG. 39.—1 and 1*a*, chromosomes in the first normal cleavage spindle of Sphærechinus; 2, equatorial plate of two-cell stage of same; 3 and 3*a*, spindles of two-cell stage of egg of hybrid of Sphærechinus by Strongylocentrotus; 4 and 4*a*, same, equatorial plates; 5 and 5*a*, hybrid of Strongylocentrotus by Sphærechinus cleavage spindle in telophase; 6, next stage of last; 7, same, two-cell stage; 8, same, later; 9, same, four-cell stage; 10, same, equatorial plate in two-cell stage (22 chromosomes); 11, same, from later stage, 24 chromosomes. (After Baltzer.)

that developed was intermediate in character; or at least showed peculiarities both of the maternal and of the paternal types. The reciprocal cross was made by fertilizing the eggs of Strongylocentrotus with the sperm of Sphærechinus. At the first cleavage of the egg some of the chromosomes divide normally, while other chromosomes remain inactive and finally be-

come scattered in the region between the others that have retreated toward the poles. When the division is completed the belated chromosomes are found to be excluded from the daughter nuclei. They appear irregular in shape and show signs of degeneration. At the next division of the egg they may still be found, but they are lost later, and seem to take no part in the development. The difference between this and the other cross seems directly caused by the differences observed in the behavior of the chromosomes.

A count of the chromosomes in the hybrid embryos shows about twenty-one chromosomes. The maternal nucleus contained eighteen. It appears that only three of the paternal chromosomes have taken a regular part in the development—fifteen of them must have degenerated in the way described above. The hybrid embryos that developed were often abnormal; the few that developed as far as plutei were apparently entirely maternal in character. Since the reciprocal cross proves that the maternal characters are not dominant, the most reasonable interpretation is that, although the foreign sperm had started the development, it had produced little or no effect on the character of the larvæ, and this absence of effect would seem most probably to be due to the elimination of most of the paternal chromosomes. It might possibly be maintained that the same kind of effect produced by the egg of Strongylocentrotus on the chromosomes of Sphærechinus is likewise produced on the protoplasm introduced by the sperm. But there is here, in contrast to the case for the chromosomes,

no evidence of any abnormal cytoplasmic behavior which could account for the observed abnormal effect.

Tennent also has found that when the sea urchin Toxopneustes (♀) is crossed to Hipponoë (♂) no loss of chromatin occurs, while reciprocally some or even all of the paternal (?) chromatin is eliminated, but the character of the larvæ in the two cases does not furnish a basis for discrimination as regards the effects due to elimination.

Some experiments by Herbst also have an important bearing on the question. The eggs of Sphærechinus were put into sea water to which a little valerianic acid had been added. This is one of the recognized methods of starting parthenogenetic development. After five minutes the eggs were taken out and put into pure sea water to which sperm of Strongylocentrotus was added. The sperm fertilized a few of the eggs. The eggs had already begun to undergo some of the changes that lead to development. The belated sperm failed to keep pace with the division so that the paternal chromosomes did not reach the poles of the egg before the egg chromosomes reformed their nuclei (Fig. 40). In consequence, the paternal chromosomes formed a nucleus of their own that came to lie in one of the cells formed by the division of the egg. As a result one cell had a maternal nucleus and the other had a double, paternal and maternal, nucleus. In later development the paternal nucleus became incorporated with the maternal nucleus of its cell. Embryos were found later, in the cultures, that were on one side maternal

and on the other side hybrid in character and probably came from such half-fertilized eggs. It will be recalled that Baltzer has shown that when the cross is made in this direction both paternal and

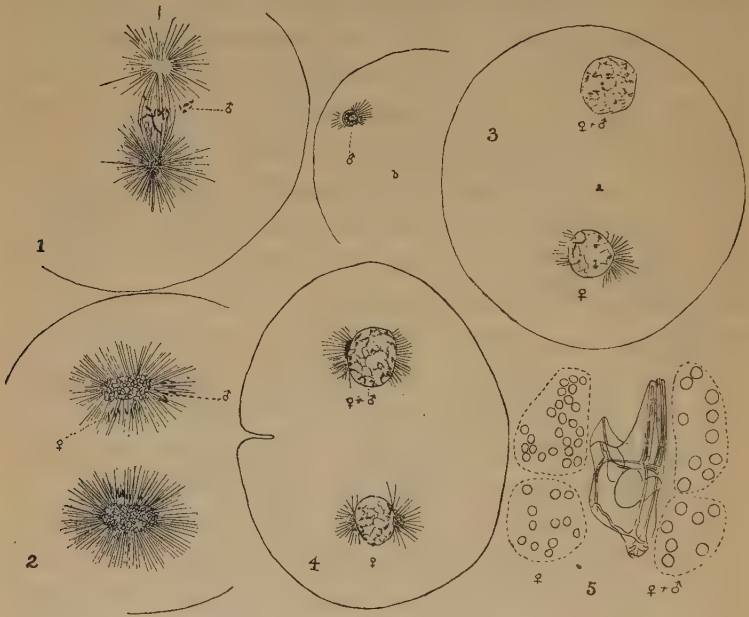


FIG. 40.—1, The chromosomes of the egg lie in the equator of the spindle, the chromosomes of the sperm at one side; 2, a later stage showing all of the paternal chromosomes lying at one side passing to one pole; 3 (to the right), later stage; the conditions are the same; there is also a supernumerary sperm in the egg (shown to the left, in another section); 4, same condition as last; 5, pluteus larva that is purely maternal on one side, and hybrid on the other. (After Herbst.)

maternal chromosomes behave normally at each division. The conclusion follows with much plausibility that the absence of paternal characters on one side is due to the absence of paternal chromosomes on that side.

The Individuality of the Chromosomes

The view that the chromosomes are persistent as individual structures in the cell has steadily gained ground during the last twenty years. The process of karyokinetic or mitotic division by means of which at each cell division the halves derived from a lengthwise split of each chromosome are carried to opposite poles, so that a genetic continuity is maintained between corresponding chromosomes (and parts of chromosomes) in mother and daughter cells, has been found to be almost universal in both plants and animals. It is true that several instances have been described in which the nucleus simply pinches into two parts, and there can be little doubt that such cases occur; but no one has been able to show in a convincing way that cells which have once divided in this manner ever return to the regular process of karyokinetic division. Case after case of amitosis that has been described for the germ cells has been either disproven, or found to rest on faulty observation, or else to relate to cells like those of the egg coats that take no part in the germinal stream.

There are several observations that lead to the view, at present generally accepted, that the chromosomes retain their individuality from one cell division to the next. These may now be given.

During the resting stage the chromosomes spin out in such a way that they appear to form a continuous network in the nucleus. They can not be identified individually during this period. When the chromo-

somes again become visible, preparatory to the next division, it has been found by Boveri in Ascaris, which is particularly well suited for the study of this point, that in sister cells the configuration of the groups of chromosomes is the same (Fig. 41). The similarity of the sister cells would be expected had the chromosomes retained during the resting stage the same shape and size and relative location that they had at the end of the last division. On no other

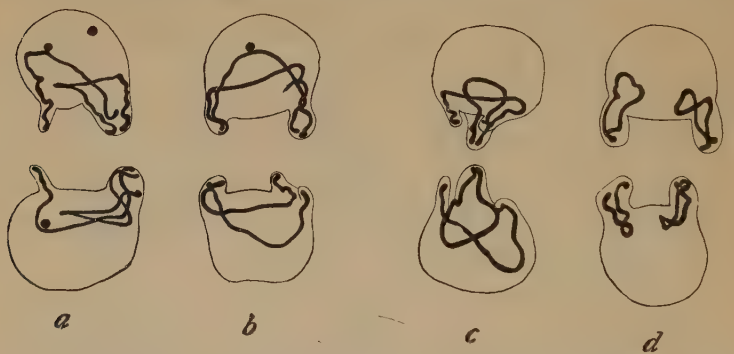


FIG. 41.—Four pairs of sister cells of Ascaris, in which the chromosomes are reappearing. Note the similarity of arrangement in the cells of each pair. (After Boveri.)

view can we so readily understand the similarities between the sister cells; for, in other cells of these same embryos that are not sister cells, a great variety of arrangements is found, and no two arrangements are so nearly alike as are those that are found in cells that have separated from each other at the last division. In a few instances certain observers believe that they have even been able to distinguish the separate chromosomes throughout the whole

resting period of the cells, but this must be received with some caution. In many animals and in some plants the chromosomes are of very different sizes and shapes, and many, or even all of them, can be identified at each division. It is found that these size relations hold throughout all divisions of the cells. While this evidence appears at first sight to show that the chromosomes are structures that perpetuate themselves, preserving their identity, yet it might be maintained, in fact it has been maintained, that each species has its own peculiar protoplasm from which chromosomes of a particular kind and number are, as it were, crystallized out anew before each cell division. This point of view can not, however, be reconciled with the evidence that follows. In Metapodius, Wilson has found that individuals may differ in the particular chromosome that he calls the m chromosome. While the normal individuals have a pair of m chromosomes, one individual had three m's; but all of the cells of any given individual have the same number. These chromosomes furnish strong support of the continuity of the chromosomes; for, in whatever number they enter the individual during fertilization, they retain that number throughout all the subsequent generations of cells. The same is true, of course, for the sex chromosomes.

Corroborative proof is found in certain hybrids, where the evidence is even more significant, because in such cases the chromosomes introduced by the male are, as it were, in a foreign medium. For example, Moenkhaus first pointed out that when

the fish Fundulus is crossed to another fish, Menidia, the two kinds of chromosomes present in the fertilized egg can readily be distinguished in later divisions. Similar observations have been made for many other crosses (Fig. 42) by Morris, Pinney, Hertwig, Federley, Doncaster, Rosenberg, etc. Despite the fact that the paternal chromosomes are in a foreign

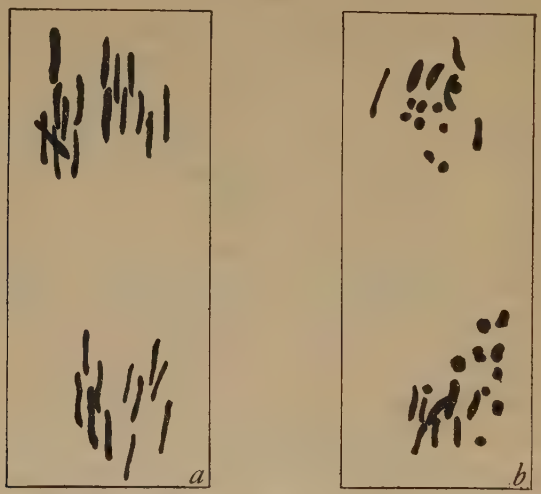


FIG. 42.—*a*, Telophase, division of an embryonic cell of Fundulus; *b*, telophase, division of an embryonic cell of egg of Fundulus fertilized by sperm of Ctenolabrus. (After Morris.)

medium they retain their characteristic size, form, and number. The embryos from these eggs are abnormal, and often die, not because chromosomes are eliminated but because the combination does not work out successfully. On the other hand, in hybrid embryos (studied by Herbst, Baltzer, and Tennent), in which paternal chromosomes are eliminated, they

seem never to re-appear subsequently, while those not eliminated always re-appear at the next cell division. Other cases of the same sort are known.

In general it may be said that even an abnormal set of chromosomes, once established in a cell, tends to persist through all succeeding cell generations. This evidence indicates that the chromosomes are not mere products of the rest of the cell but are self-perpetuating structures.

The Chromosomes during the Maturation of the Germ Cells

On the most essential point concerning the maturation of the egg and sperm there is no dispute: the observed number of chromosomes is reduced to half. It is generally agreed that this lowering of the number is due to the union of similar chromosomes in pairs, each chromosome derived from the father conjugating with the homologous chromosome derived from the mother. In cases where different chromosomes can be distinguished by their shape or size relations, the relations of these pairs correspond exactly to what they should be if like chromosomes conjugated.

When we come to consider how this union of chromosomes is brought about, there is much divergence of opinion, for the evidence is fragmentary or contradictory on almost every point. The reason for this uncertainty is clear: the stages at which the reduction in the number of the chromosomes takes place are extraordinarily difficult to interpret, be-

cause at this time the chromosomes are in the form of what seems to be a dense tangle of long threads. When this stage has been passed through, and the chromosomes are distinguishable again, the pairing has been completed. For any information that is worth while we have to rely on the best material available. It may be disputed which material is the best, but it will be generally conceded that a few types have shown themselves superior to others. The account of maturation that is here followed confines itself to two types—one for the male and the other for the female. These are selected cases, it is true, but they are those that give, in the opinion of the writers, two of the most complete accounts of these stages. The selection is admittedly not without bias, for these types can be most advantageously utilized to illustrate how crossing over can take place between the members of homologous pairs of chromosomes.

The salamander, Batracoseps attenuatus, has furnished some of the best material for the study of the ripening of the germ cells of the male. The account that follows is taken from Janssens' elaborate and detailed study of the spermatogenesis of Batracoseps.

At the end of the multiplication period (spermatogonial divisions) the nucleus appears as shown in Fig. 43, *a*. It then passes into a condition resembling a resting stage, *b*. Later the chromosomes begin to emerge in the form of long thin threads as shown in *c*, *d*, *e*. In the last figure (the leptotene stage) the ends of the thin threads are directed toward one pole

where some of the ends can be seen to be arranged in pairs. As they unite in pairs these thin threads often have the appearance of twisting tightly around

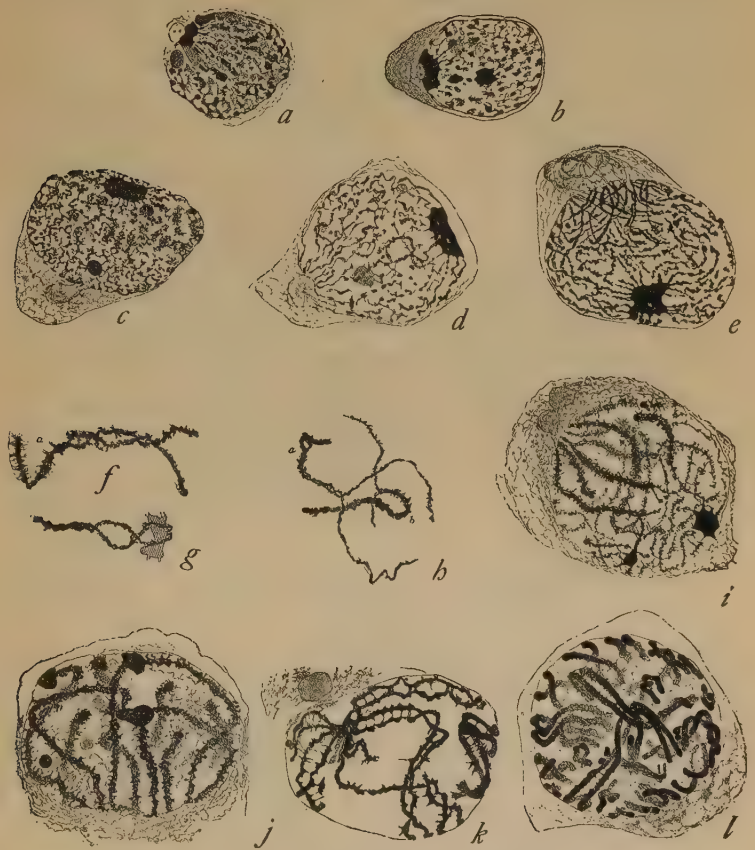


FIG. 43.—Spermatogenesis of Batracoseps attenuatus. *a*, late telophase of spermatogonial division; *b*, resting stage after the last spermatogonial division; *c*, appearance of the spireme; *d* and *e*, later stage of last (bouquet grele); *f*, *g*, *h*, twisting of leptotene threads around each other (amphitene stage); *i*, amphitene stage (entire cell); *j*, pachytene stage (bouquet pachytene); *k*, longitudinal splitting of threads (strepsinema stage); *l*, shortening and thickening of the chromosomes. (After Janssens.)

each other, beginning at the end where they first approached each other. The details of the union of the threads are further shown in *f*, *g*, *h*. As they unite they contract until they are in the form of a thicker thread, as seen in *i*, where the process of fusion has progressed as far as the middle of the nucleus. Later, *j*, the threads become fused throughout their length (pachytene stage). Still later the thick threads begin to show a longitudinal split (diplotene stage), and cross connections, uniting the halves of the threads, appear in different places. The threads thicken until finally a stage is reached like that shown in *k*, which, by further contraction, reaches the condition shown in *l*, a stage preparatory to the first maturation division. The threads of each pair, in all the stages of the latter part of the diplotene stage, are much twisted around each other; they are now so thick that they show the twisted condition very plainly.

The egg undergoes a series of changes during its maturation which parallels those of the sperm, and which leads also to the reduction in the number of the chromosomes to half of the full number. The eggs of a shark (Pristiurus melanostomus) have been described by Maréchal as passing through the following stages. At the end of the period of multiplication the eggs pass into a resting stage (Fig. 44, *a*) in which the chromatin appears as a delicate reticulum. A later stage is shown in *b*, *c*, when the separate thin threads begin to make their appearance, and take parallel courses, *d* (leptotene stage). These

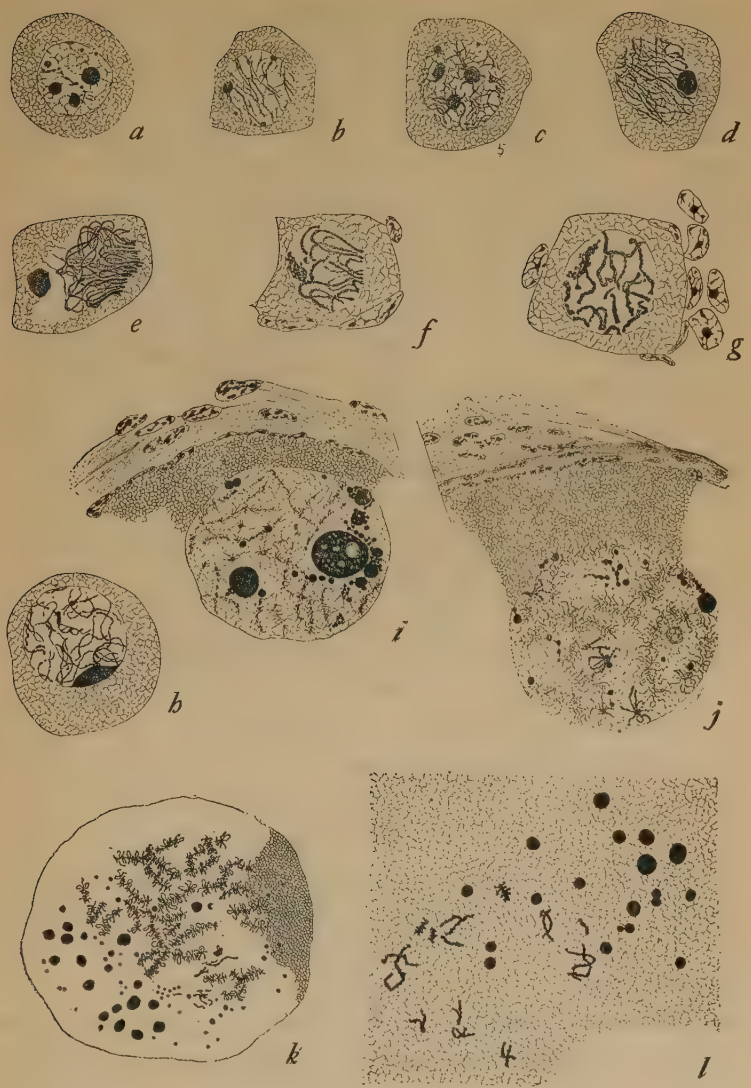


FIG. 44.—The growth, synapsis, and reduction stages in the egg of Pristiurus melanostomus. (After Maréchal.)

thin threads next assume the form of loops with their free ends pointing toward one pole, *e* (bouquet stage, also called the period of synapsis). At their free ends the threads soon appear to meet in pairs, *d* and *e*. Each pair, by the apparent fusion of its threads, leads to the formation of a thick thread in the form of a loop, *f*. Further condensation and separation of the threads leads to the condition shown in *g*. The thick double threads next show a lengthwise split, the halves being often twisted around each other (diplotene stage) *h*. The pairs of threads now begin again to become longer and to occupy more of the interior of the nucleus as seen in *i*. The eggs have grown larger meanwhile and the yolk appears. As the nucleus grows still larger, keeping pace with the growth of the cell, the chromosomes begin to lose their staining capacity. Despite the difficulty of tracing the chromosomes throughout the remaining period, Maréchal has succeeded in following them, step by step. His drawings of the chromosomes give the impression of the existence of a central core or filament remaining, as shown in Fig. 44 *i*, *j*, *k*. Delicate loops and threads are attached to this core and may be traced out into the region of each side of the chromosome. During these stages deeply staining balls of material, the nucleoli, appear in the nucleus. Finally the chromatin threads begin to condense again and once more take the stain; the chromosomes are found lying in pairs often twisted around each other as before, as seen in *l*. They pass in this condition on to the first

polar spindle, which develops in the egg as the nuclear membrane breaks down.

At or before the time when the double chromosomes of the sperm and of the egg pass onto the

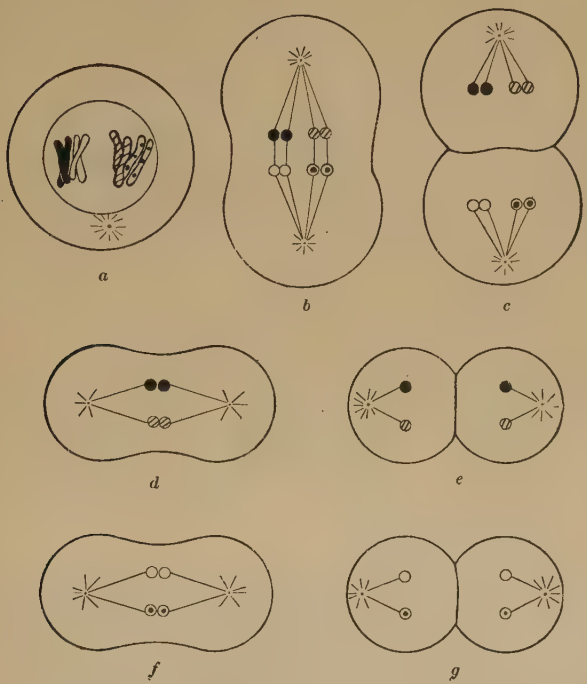


FIG. 45.—Diagram to illustrate the two reduction divisions of spermatogonial cells. *a*, first spermatocyte with two tetrads; *b* and *c*, division of last; *d* and *f*, division of two cells of *c*; *e* and *g*, completion of second division.

first maturation spindle, each half of the double chromosome splits lengthwise so that four parallel strands are present (Figs. 45, 46). One of the two longitudinal splits in the tetrad is generally thought

to correspond to the former line of union of the conjugating threads (reductional split); the other split is then said to correspond to a division within each thread (equational split). It is obvious, however, if crossing over has previously taken place between the threads, or between strands only, that these distinctions apply rather to segments of the chromosomes than to the chromosomes as wholes.

These two splits are in preparation for the two maturation divisions that usually take place in rapid succession, without an intervening resting stage. It is customary therefore to look upon the second lengthwise split as a precocious split in the chromosomes preparatory to the second division. If the reduction in the number of the chromosomes to half of the original number were the sole object of the reduction divisions, one division would suffice to separate the two chromosomes of a pair that had united and it is not apparent why there should be a second division at all.

The two maturation divisions with tetrad formation are typically illustrated in the changes that take place in the spermatogenesis and oögenesis of Ascaris, the thread worm of the horse, as worked out by van Beneden, Brauer, O. Hertwig and others. In one variety four chromosomes occur which become reduced to two; hence there are only two tetrads present (Fig. 45, *a*). At the first division two halves of each thread move to one pole and two to the other as in *b* and *c*. At the second division the separation of the two remaining threads takes place,

d and *f*. At the end of the process there are two chromosomes remaining in each of the four cells, *e* and *g*. Each cell becomes a spermatozoon. Here as in most cases there is nothing to show whether the first division is reductional and the second equational, or the reverse. There is much divergence of opinion on this point for different species. The end

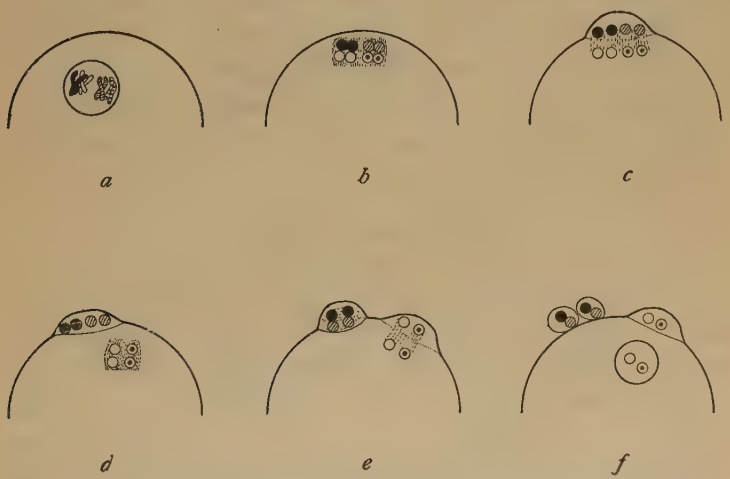


FIG. 46.—Diagram to show the extrusion of the two polar bodies. Two tetrads are represented in *a*. The two succeeding divisions *b-c*, *d-e*, show the separation of the members of the tetrads with the result that one of each kind is left in the egg.

result, however, is the same so far as the genetic problem is concerned, the sequence being ordinarily a matter of no significance.

In the egg (Fig. 46) the process is identical with that in the sperm, except that one of the two cells formed is much smaller than the other. The small cell is the polar body. At the first division the nucleus

sends out half of its chromatin into the first polar body (Fig. 46, *c*). Without a resting stage a new spindle is formed around the chromosomes in the egg and a second polar body is thrown off, as in *e*. The first polar body may also divide. The three polar bodies and the egg, *f*, are comparable to the four spermatozoa. All four spermatozoa are functional, but only one product of the two divisions of the egg is functional. Unless the tetrad is specifically oriented upon the polar spindle of the egg the chance is equally good that any one of the four threads that make up the tetrad will be the one that remains in the egg.

Crossing Over

If the traditional view of the maturation of the egg and of the sperm were accepted as covering the entire behavior of the chromosomes during this period, there would be no possibility for an interchange between the members of a pair. But there are several stages in the ripening of the germ cells when an interchange between homologous chromosomes might possibly take place. For instance, when the thin threads are coming together (Fig. 43, *e*, *f*, *g*, *h*) several observers have described them as twisting around each other (synaptic twisting) as represented in these figures. If where the threads cross a part of one thread becomes continuous with the remainder of the other thread (Fig. 24) an interchange of pieces will have been accomplished. If, as shown in Fig. 24, *B*, the chromosomes are represented as a linear

series of beads (chromomeres), then, when the conjugating chromosomes twist around each other, whole sections of one chain will come to lie, now on one side, now on the other side, in the double chromosome. If, when the two series of beads come to separate from each other, all of the segments that lie on the same side tend to go to one pole, and all of those on the opposite side to the other pole, each series must, in order to separate, break apart between the beads at the crossing point. Moreover, since the essential part of the process is that homologous beads go to opposite poles it follows that the break between the beads of two chains must always be at identical levels. It is not necessary to assume that crossing over takes place at every node, but only that it may sometimes take place. In fact, our work on Drosophila shows for the sex chromosome in the female that crossing over takes place in only about half of the cells, and double crossing over is a rather rare event.

There is a later stage also at which crossing over might be supposed to take place. After the thin threads have conjugated to form the thick threads, and these have shortened and split lengthwise, four strands are present (Fig. 47). If two of the strands fuse at the crossing place (the pieces of one strand uniting endwise with the pieces of the other) crossing over is brought about. It is this type in particular that Janssens named chiasmatype. In support of this method of crossing over are Janssens' observations on Batracoseps, where he concludes from the

method by which the strands are found joined at the time when they draw apart, that cross union of the threads must have previously taken place.

If crossing over be supposed to take place between two single threads (Fig. 24) all four gametes that ultimately result from such a cell will be crossover gametes. On the other hand, if crossing over takes

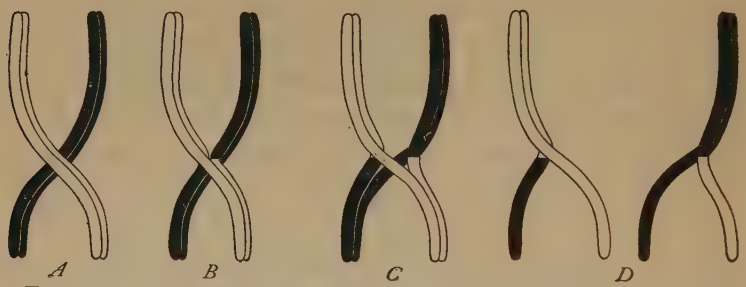


FIG. 47.—Four stages in crossing over, according to the "typical" chiasma type of Janssens. The white rod and the black rod are each split lengthwise; crossing over takes place only between two of the four strands.

place by means of the chiasmatype (Fig. 47) only two of the resulting four cells will be crossover gametes, the other two being non-crossover gametes.[1]

Looked at from the point of view of the total output, there would be no way in which to tell whether one or the other of the above processes has taken place; although the formation of a given number of crossover gametes involves only half as many participating cells in the case of the single thread type as in the case of the double thread type.

[1] If, after the thick threads have split, crossing over involving *both* strands of each chromosome should take place, instead of only one strand as in the chiasmatype, sensu strictu, all four gametes that result would be crossover gametes.

At present it seems better not to attempt to commit the theory of crossing over to one rather than to another of these stages; for, whether the process occurs at the leptotene thread stage as suggested above, or, as Janssens believes, at a later stage (strepsinema), the genetic result is the same. What we wish to point out is that in the phases through which the chromosomes pass at the maturation stages there is given an opportunity for an interchange of parts. The genetic evidence shows very clearly that interchanges do take place, as is best illustrated in the case of the sex chromosomes, whose history can be traced with some assurance from one generation to the next.

What we wish especially to insist upon and emphasize is that the evidence from linkage in Drosophila has shown beyond any doubt that crossing over is not a process that involves only a particular factor in relation to its allelomorph. Our work has shown positively that there is a tendency for large sections of the chromosomes to interchange whenever crossing over occurs.

Another idea that is likely to suggest itself in this connection has also been disproven by the evidence from Drosophila. It might be supposed that at a resting stage the chromosomes go to pieces and the fragments come together again before the next division period. Linkage might then mean the likelihood of fragments remaining intact, etc. But if the chromosomes broke up completely into their constituent elements at each resting period then

there is no explanation as to why the factors in a group remain together in sections as explained on page 66. If it is supposed that the chromosomes break only once or twice, and that linkage represents the holding together of the pieces, then one is forced to assume that the breaking up is the same in both members of a pair, yet entirely inconstant in different cells; for otherwise the reunion of the fragments would lead to duplication or loss of whole sections of the chromosomes, and all order would soon be lost. A large amount of data relating to sex linked characters has shown that the sex chromosomes must remain intact as often as they break apart, and even when they break apart this takes place, as a rule, at only one place.

Other Theories of Crossing Over

The "reduplication" theory of Bateson and Punnett has been treated in another section (see page 74) and the discussion need not be repeated here.

It has been claimed by Goldschmidt that, even though the groups of factors are admitted to be carried in the chromosomes and to undergo some sort of interchange before reduction, it is not necessary to assume that this interchange is of the nature of a crossing over of the threads. He has postulated that during resting stages the genes are set free from the forces that hold them in their places in the chromosomes, and that when they reassume their places before division the two allelomorphs may

sometime be found to have exchanged places in the pair of chromosomes. Such interchange of genes is due to variations in the strength of the specific forces attracting each back to its place in the original series, and is supposed to occur in a specific proportion of cases, which is different for different pairs of genes. The insufficiency of this hypothesis becomes evident when we remember that whole sections of the linear series are interchanged bodily, a single pair of genes never interchanging alone. There is the further point that after crossing over has taken place the same percentage of interchange is found in the next generation as occurred previously, a condition which is the reverse of that which would result on Goldschmidt's hypothesis.

Castle's suggestion that the genes are arranged in a three dimensional manner was arrived at by combining linkage results obtained in different experiments. It is well known that such results are not strictly comparable. When data from a single experiment involving many loci at once are used, all the linkages of the factors are most nearly represented by the distances of points in a curved line lying in a single plane, instead of in three dimensions. Further analysis shows that the curvature of this line is due to multiple crossovers, which have been omitted from the calculation of the longer distances. When these corrections are made the curved line of course resolves itself into a straight line. Castle has now withdrawn his hypothesis of three dimensional arrangement.

Special attention must be called here to two facts which have been repeatedly pointed out above, and which have long been commonplaces in the literature on linkage in Drosophila. First, owing to the existence of multiple crossing over, it is *not* true that the distances between the factors in the straight linear map have the same numerical values as the observed percentage of recombination. Secondly, owing to the reduction in the amount of multiple crossing over caused by interference, it is *not* true that the relation between map distance and recombination is that which would result if crossings over were independent of each other ("Trow's formula" assumed a relationship of linkages of this sort, but it had already been disproved in Drosophila). Haldane has recently restated the evidence against these misconceptions in slightly different terminology, under the erroneous impression that the first of the misconceptions is held by Drosophila workers. In substitution for these two views he proposes an empirical formula to express the relation supposedly existing between distance and separation frequency. Such an attempt to find a general formula is futile, for it has been proved that the relationship between map-distance and observed percentage of crossing over is different not only in different chromosomes, but even very strikingly in different regions of the same chromosome. The only satisfactory representation of such relationships is one that gives for each chromosome and for each region of that chromosome the observed relation

between map-distance and crossover values. From such careful, detailed, region-by-region studies a more general statement and formulation should emerge. Until such studies are completed there is nothing to be gained from *a priori* attempts to formulate the relationship. The Drosophila workers had studied the possibilities of such formulæ and had worked out several that applied under diverse conditions. Such formulæ were recognized as too partial and tentative to be worth publication as yet. Moreover, it is evident from the foregoing that within a given region the exact function of distance represented by crossover values depends directly upon the magnitude of the interference acting at each given distance. The amount of interference may be expressed by the index called "coincidence," which is obtained by dividing the number of double crossovers actually observed by the number that would be expected if crossings over were independent of one another. Several series of results relating distance and coincidence have already been published, but it will require extended and special experimentation before the relationship for each region can be precisely determined. A formula for the relation of distance to linkage has little meaning in reference to the underlying chromosome processes unless thus expressed, in terms of the actual coincidences involved.

Attachment of Sex-Chromosomes to Autosomes

If one or more genes for sex are present in a chromosome, that chromosome would be designated as a sex chromosome, but in order that the mechanism give a differential result such chromosome must be present in duplex (XX or ZZ) in some individuals and simplex (X or Z) in others. It is not necessary in the simplex individual that one whole chromosome be absent, but only that one should lack factors for sex, as in the case of Y-chromosome in one type, and supposedly the W-chromosome in the other.

There is still another situation in regard to the chromosomes that carry the sex genes. In a few cases there is more than a suspicion that they are attached to other chromosomes, or what amounts to the same thing,that the region of the chromosomes bearing sex determining genes lies at one end of an ordinary chromosome. In such cases two of these chromosomes with attached portions are supposed to be present in the female (the XX type), but in the male only one chromosome of the pair has the attached portion. The thread worm, Ascaris, is a case in point. It has been observed by Boveri, Boring, Frolowa, Mulsow, Kautsch, and Geinitz that occasionally one or two small detached pieces of chromosomes are found constantly present in certain individuals—pieces that show a tendency in certain cells to become attached, or associated

with a pair of ordinary chromosomes. These pieces have been supposed to be the sex chromosomes. Their inconstancy and some apparent irregularity in their distribution when the polar bodies are formed has thrown some doubt on that interpretation.

Perhaps more significant are the observations of Kautsch and Geinitz on the number of chromomeres into which the somatic chromosomes of Ascaris are resolved. It appears in some individuals (females?) there are about 8 more of these than in other individuals (males?). This relation might be expressed as follows:

52 chromosomes in male = 22 + 8 (egg) + 22 (sperm)

60 chromosomes in female = 22 + 8 (egg) + 22 + 8 (sperm)

Kautsch has suggested that the 8 chromosomes are attached at the ends of one of the pairs of chromosomes and are set free normally only when the chromosomes break apart into their constituent chromosomes. In the female two such chromosomes would be present, in the male only one member of the pair would have the attached part. The results would then conform to the ordinary XX—XY mechanism. The only objection to such a view is that at an early stage the ends of the chromosomes that go to the somatic cells appear to slough off. If this involved the sex region, the sex determining mechanism would be lost in the soma. But there is some evidence that the sloughing off does not include essential elements of the chromosomes; for,

in other nematodes, where many small chromosomes are present, such a loss has been observed from all of the chromosomes, which nevertheless retain their constancy of number in the germ cells.

It is not without interest to find in these Nematodes with many small chromosomes that the female and the male have constantly different numbers of chromosomes (Edwards, Gulick, Schleip) —the additional ones corresponding to the extra chromosomes of Ascaris. Thus Edwards finds in Ascaris lumbricoides:

43 chromosomes in the male = 19 + 5 (egg) + 19 (male producing-sperm)

48 chromosomes in the female = 19 + 5 (egg) 19 + 5 (female producing-sperm)

In Ascaris incurva, Goodrich has shown (Fig. 36 *M*) that a sex chromosome complex consisting of 7 X-chromosomes goes to one pole of the spindle, so that the female-producing sperm has 21 chromosomes; and the male-producing only 14. At the time of reduction the X-chromosome complex of 7 elements shows a tendency to unite more or less into a compound element (Fig. 36 *M*).

Tetraploidy

The fact that "pairs of species" are known, one characterized by having twice the number of chromosomes of the other, has suggested that new types may arise through doubling of the chromosome number. The double chromosome types are larger

and have larger cells than the type from which they may be supposed to have arisen. The most important consideration in this connection is that since through tetraploidy the number of genes is doubled, opportunity is given by further mutation in these genes for an indefinite increase in the number of genes in the course of evolution. This possibility suffices to meet the paradox stated by Bateson, that there may have been no increase in the number of genes in the course of evolution from "amoeba to man." Bateson suggested as a possibility that all that has happened in the course of evolution has resulted from the dropping out of some of the original genes. While "evolution through loss of genes" cannot be refuted as an abstract contention, however improbable, it would still leave unsolved the whole question as to the origin of the genes present "at the beginning." Such a speculation rests nominally on an hypothesis concerning the nature of mutation itself (loss of a factor).

In a few cases tetraploidy has arisen in pedigreed material, and in two cases it has been induced artificially. In the evening primrose, Oenothera, a tetraploid form occasionally arises. It has been called by its discoverer De Vries, O. gigas. The original type O. Lamarckiana has 14 chromosomes and O. gigas 28. Stomps has calculated that it occurs only once in about 100,000 times. Several possible ways in which it arises have been suggested. First, that it arises after fertilization through division of the chromosomes of the zygote unaccompanied by

nuclear and cell division. Second, that it comes from the union of two gametes each with the unreduced number of chromosomes. Third, that such plants do not arise from the egg itself, but as bud sports from cells that had the diploid number of chromosomes. There is somewhat better evidence in favor of the second view than of the other two. Whatever its origin, O. gigas breeds true in the same sense as does the parent type, its germ-cells having the double number of chromosomes after reduction.

Gigas forms of Primula have appeared under cultivation. Gregory has found some of these to have tetraploid chromosomes. In other cases a giant has appeared as a bud sport in the hybrid form Primula Kewensis.

Tetraploid individuals have been artificially produced in mosses by the Marchals. In mosses there are two generations that alternate—the sexual generation that produces eggs and sperm, and the sexual spore-bearing generation that arises from the fertilized egg. The cells of the sexual moss-plant, as well as the egg-cells and sperm that it produces, have the haploid number of chromosomes. After fertilization the egg contains the diploid number of chromosomes, and since it gives rise to the sporophyte, this also has the diploid number of chromosomes in all of its cells. The spores are formed by two divisions, and one of them must be a reduction-division, since each spore has the haploid number of chromosomes.

The tissue of the sporophyte is capable of regenerating if a piece of it is kept under proper cultural conditions. Its cells do not regenerate another sporophyte but instead a sexual moss-plant, or gametophyte, which now has the diploid number of cells, since it arose directly from sporophyte tissue. These diploid gametophytes give rise to antherozoids (without reducing) and to female oospheres (without reducing). Therefore by the union of the two a tetraploid sporophyte is produced. In a few mosses, octuploid sporophytes have been produced, by starting with a tetraploid sporophyte and repeating the procedure just described.

Tetraploid plants of the tomato (Solanum lycopersicum) and of the nightshade (Solanum nigrum) have been artificially produced by Winkler by means of the same kind of grafting experiments that had produced periclinal chimaeras in his earlier work. A piece of the nightshade was grafted onto a tomato stock by a wedge-shaped union. After union had taken place the combination was cut across at the level of union in such a way that the tissue of the nightshade was exposed on each side of the cut surface and that of tomato in the middle of the surface. If at the same time all the axial buds were removed from such a piece new adventitious buds appeared on the cut surface. Most of these gave rise to plants that were either nightshades or tomatoes, but rarely a bud arose that had a core of tomato tissue and a skin of nightshade

(periclinal chimaera), or a bud with the reverse relations, namely, nightshade core and tomato skin. Still another kind of bud also rarely arose, namely, one that was tomato on one side (or in one section) and nightshade on the other (sectorial chimaera). In one instance a periclinal chimaera arose that was a giant, and which Winkler showed was tetraploid. It had a core of tomato cells that were tetraploid, and a skin of nightshade. Winkler got rid of the skin by cutting the stem of a young plant across and removing its axial buds. The adventitious buds that developed from the callus over the cut end were in some cases composed entirely of tomato cells, both in core and skin. Such plants were pure tetraploid giants.

The cells of the ordinary tomato contain 24 chromosomes (Fig. 47*A*, *b*), the pollen mother cells contain the reduced number of chromosomes (Fig. 47*A*, *a*). The tissue cells of the giant contained 48 chromosomes (Fig. 47*A*, *d*), and the pollen mother cells 24 chromosomes (Fig. 47*A*, *c*). How the original doubling of the number of the chromosomes comes about in cases like this one is unknown. It may have arisen by two cells fusing at the cut surface into a single cell that formed the growing tip of a new plant, or a tetraploid cell may have arisen by a direct doubling of the number of chromosomes in a cell as a result of the failure of the cell to divide after the chromosomes had divided. Since giants never appeared from a callus or from adventitious buds, except in cases where grafting

had first occurred, Winkler is inclined to ascribe the results to some special conditions that are thus introduced.

In somewhat the same way Winkler obtained a giant nightshade plant. The ordinary cells of the

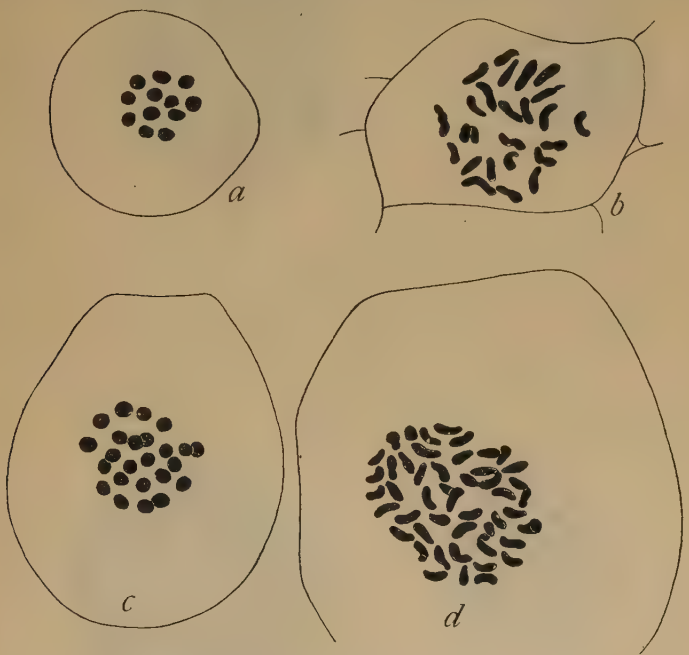


Fig. 47A—Chromosomes of normal and of giant tomato. *a*, pollen mother cell of tomato with 12 chromosomes. *b*, somatic cell of tomato with 24 chromosomes. *c*, pollen mother cell of giant tomato, with 24 chromosomes. *d*, somatic cell of giant tomato with 48 chromosomes. (After Winkler.)

nightshade contain 72 chromosomes (Fig. 47*B*, *b*), and the pollen mother cells 36 chromosomes (Fig. 47*B*, *a*). The cells of the giant nightshade contained 144 chromosomes (Fig. 47*B*, *d*), and the

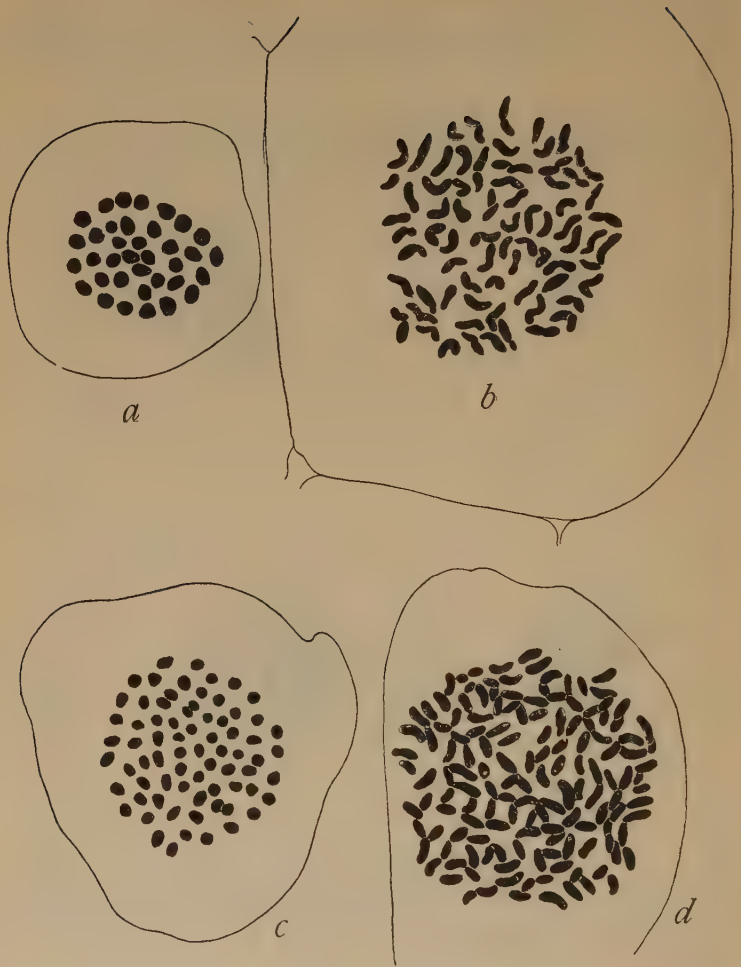


Fig. 47B.—Chromosomes of normal and of giant nightshade. *a*, pollen mother cell of nightshade, with 36 chromosomes. *b*, somatic cell of nightshade, with 72 chromosomes. *c*, pollen mother cell of giant nightshade, with 72 chromosomes. *d*, somatic cell of giant nightshade, with 144 chromosomes. (After Winkler.)

pollen mother cells 72 chromosomes (Fig. 47*B*, *c*). Both of these giant plants were larger than the normal plant; they grew more vigorously and all of the cells were larger. The difference in size extends to the flowers, to the pollen, stomata, trichomes, etc., and even the starch plastids are larger. This latter condition seems anomalous, but Winkler states that even in normal plants the size of these plastids varies with the size of the cells containing them.

CHAPTER VI

CYTOPLASMIC INHERITANCE

When a sperm, bearing a known dominant gene for an embryo-character, fertilizes an egg, the embryo may show only the recessive character of the mother's race. The rate of cleavage of the egg is a case in point. These results are explicable, because the egg cytoplasm has already developed under the influence of the duplex maternal chromosomes. On the other hand there may be self-perpetuating bodies in the cytoplasm of the egg that are responsible for certain characters, such as the chlorophyll plastids. Both of these phenomena are here described as cytoplasmic inheritance.

The interpretation of Mendelian inheritance on a chromosomal basis by no means excludes the possibility that there may be other forms of inheritance depending on other cell materials. Although the cytoplasm is essential for the development of the organism, and is transmitted by the egg to each new generation, its substance does not perpetuate itself unchanged as do the chromosomes, and it is therefore really not inherited. There are, however, certain bodies carried by the protoplasm, such as plastids (possibly also chondriosomes), which, like the chromatin, are able to grow and divide, and hence might have the power to perpetuate themselves unchanged

indefinitely. Such bodies might not only produce passive products, like starch or pigment, but even active enzymes, which, interacting with other products of development, might determine the characteristics of the race.

Structures like the shell and the yolk of eggs are purely maternal in origin, but since they do not have the power of growth and division, they are not able to perpetuate themselves indefinitely, nevertheless they may determine certain characteristics of the embryo, and to this extent may appear to influence the hereditary characters of the generation to which the embryo belongs. For instance, the females of certain races of silkworm moths have white eggs, because the shell is white. If such eggs are fertilized by sperm of another race, that has eggs with a dominant green colored shell, the shells are nevertheless white. Conversely when the green eggs of a female moth of the green egg race are fertilized by the sperm of a male of a white egg race, the color remains green. When the moths develop from either of these two kinds of hybrid eggs, one white, one green, they lay only green eggs, because in the hybrid the factor for green dominates and determines the color of the shell that is produced in the new eggs. These green eggs give rise to moths, three of which lay eggs that are green to one that lays eggs that are white, showing that here there is only the ordinary case of Mendelian inheritance, which is obscured, however, when the characters of the young embryo are considered, because, as has been shown, these

characters are due to peculiarities of the eggs before they are laid.

The serosa on the other hand is a cellular membrane that develops around the embryo and produces pigment. The pigment seen through the shell gives the embryo a definite color, which in the hybrid embryo is characteristic of the maternal race. Since the serosa pigment is not present in the egg, but develops after fertilization the inheritance here appears to be determined by the character of the egg and not by the sperm. But the genetic history of this character of the embryo is apparently the same as that of the color of the shell or of the yolk. It can, therefore, be interpreted in the same way. There must, then, be present in the egg some substance that is at first uncolored, and later this substance when carried into the serosa produces pigment, presumably by interacting with something else there. In the next generation, however, the influence of the father comes to light when the F_2 embryo produces its serosa material; for now the nucleus of the P_1 male has had opportunity to determine what this material may be, and should the paternal factor be the dominant one it determines the kind of material that the eggs will contain and hence the color of the serosa of this new generation.

A case of cytoplasmic inheritance has been described by Correns in the four-o'clock, Mirabilis jalapa. There is a race whose leaves are checkered with green and white, but some branches may have leaves entirely green, other branches may have only

white leaves. If the flowers of the green branches are self-fertilized, the young plants are green. If the flowers of the white branches are self-fertilized, the offspring have white leaves and these plants perish for want of chlorophyll. From the checkered branches the offspring may be green, or checkered, or white.

When a cross is made between the flowers borne by branches that are unlike, the inheritance is purely maternal. For example, if the pistil of a white branch is fertilized with pollen from a pure green plant, only white leaved offspring are produced. The reciprocal cross, the pistil from a green branch fertilized with pollen from a white branch, gives only green offspring, and these remain green through all subsequent generations.

Correns points out that these results can be interpreted if the whitening is due to a sort of disease that is carried by the cytoplasm. The egg cytoplasm carries over the disease to the next generation. As the pollen does not bring in any cytoplasm the disease is not transmitted through the male side.

Baur points out that in several other plants in which varieties with leaves marked with white exist, as in Melandrium, Antirrhinum, etc., the inheritance is strictly Mendelian, for the F_1 generation is green and the F_2 generation is made up of three greens to one marked with white. In these cases the color may depend on a chromosomal factor. But there is a case in Pelargonium that Baur thinks can not be explained in either of the foregoing ways. Here

again there are mosaic branches, white branches, and also green branches. Flowers on green branches crossed with flowers on white branches give mosaic plants, irrespective of which way the cross is made. A self-fertilized flower from a green branch gives rise to a plant with purely green leaves. If a flower from a checkered branch is self-fertilized it produces a checkered plant. If a flower from a white branch is self-fertilized it gives rise to a white plant.

Baur suggests tentatively, the following hypothesis to explain the case of Pelargonium. The green color of this plant, like that of all flowering plants, is due to chlorophyll grains and these grains multiply, supplying all the cells in generations that subsequently arise with their quota of grains. In the white parts these grains are defective in the sense that they fail to produce the green color, but retain their power of multiplying. If now it is assumed that the pollen as well as the egg may transmit some chlorophyll grains the results can be explained. For, in the division of the cells that contain both green (normal) and white (abnormal) grains there will arise at times an unequal distribution of the grains, and in extreme cases two kinds of branches may arise, one with green and the other with white grains. The hypothesis calls for transmission through the cytoplasm of the pollen as well as through that of the egg cell. Baur states that until this fact can be established the interpretation must be uncertain.

CHAPTER VII

THE CORRESPONDENCE BETWEEN THE DISTRIBUTION OF THE CHROMOSOMES AND OF THE GENETIC FACTORS

Attention has been called to the fact that paired factors are distributed in the same way as are homologous chromosomes, and that factors which are assorted independently are distributed in the same way as non-homologous chromosomes. In proof of the latter point there is Wilson's evidence for a Metapodius with three homologous m-chromosomes. It was found that the extra m goes to the gamete that receives X as often as to the other gamete. Miss Carothers describes in detail several cases in the spermatogenesis of grasshoppers where the distribution of chromosome pairs with unequal members shows complete independence between pairs. Not only are the pairs of factors assorted independently, as are the chromosomes, but in Drosophila, where the number of independently assorting groups of factors has been determined, it has been found that the number is identical with the number of chromosome pairs. Moreover, even the relative sizes of the groups—both as determined by the *number of factors* they contain and by the *frequency of crossing over* within them—are the same

as those of the chromosomes. Finally, the distribution of the factors within any one group is what the chromosome hypothesis calls for. For the frequencies of separation (or combination) between the different factors of a group are in a linear relation to each other, and the relation is even specifically of such a type (involving interference) as would be expected to occur if the separations between the factors resulted from the crossing over between two twisted chromosomes which the cytological evidence indicates may occur.

Even in cases where the chromosomes are not distributed in the usual way it is found that the factors have the same unusual method of distribution. For example, in moths there are some cases of extraordinary interest because the chromosomes can be traced to and through the ripening period of the eggs of the hybrid. Certain species of the moth Pygæra that have different numbers of chromosomes were crossed by Federley. The full number (calculated) and the reduced number of chromosomes in the different species are as follows:

	Diploid	Haploid
P. anachoreta	60	30
P. curtula	58	29
P. pigra	46	23

In the hybrids, the full number is the sum of the two haploid sets that went in from the parents. This shows that the chromosomes preserve their individuality through many successive cell divisions in a

foreign cytoplasm. In the maturation a few of the chromosomes seem at times to unite in pairs, but most of them fail to do so, so that while the number of the chromosomes at the first maturation division is slightly less than the full number it is much more than half of that number. Different types of hybrids behave slightly differently in respect to the extent to which union in pairs takes place. The failure to unite indicates that in normal maturation homologous chromosomes mate with each other, for here there are few or no chromosomes that are strictly homologous and yet there is just as much opportunity as in normal maturation for non-homologous chromosomes from the same parent to unite.

When the first spermatocyte division takes place in the hybrid, all the unmated chromosomes divide, but the few chromosomes that are mated presumably separate. Consequently each of the daughter cells has the double number of chromosomes (a set from each parent species), except for the few chromosomes that had been united in pairs. At the second maturation division the chromosomes again divide, so that the spermatozoa too should receive nearly the double number of chromosomes, one set from one species, the other set from the other species.

If, then, the factors are contained in the chromosomes, we should expect that, except for any factors in the few chromosomes that mate and separate, the hybrid would transmit to all its offspring the same

factors, since every spermatozoon receives, with the above exceptions, all the chromosomes (paternal and maternal) that the hybrid contains. On crossing the hybrid to either parent, it is found that the offspring actually are very much alike, *i.e.*, have all received practically the same factors—a striking contrast to the result usually obtained in "backcrosses." In respect to just one character (a larval marking), however, the above relation does not hold, but ordinary Mendelian results are obtained, and this in turn corresponds with the fact that a few chromosomes do undergo segregation. In regard to the other characters, not only are the offspring like each other, but they resemble the hybrid more than either of the pure species, corresponding with the fact that they contain complete sets of chromosomes from both types. But they do not look just like the F_1 hybrid, and correspondingly one set of chromosomes is in the diploid, the other in the haploid number. This is because they receive a set of one species from both parents, but a set of the other species only from the hybrid parent. Federley also shows that when maturation takes place in this triploid individual one set of chromosomes does not undergo mating, but the others—presumably those in the two identical sets—do pair with each other, so that the total number is reduced to one bivalent set, and one single set. If the paired chromosomes separate and the unpaired ones divide, as occurs in the F_1 hybrid, the double number of chromosomes, a set of each species, will again be found in the sperm, as was the case in the first hybrid. In other

words there is expected no return to either parent type, but the hybrid when backcrossed always continues to produce hybrids. Moreover, there is no apparent weakening or other influence exerted by the egg on the foreign chromosomes even in successive generations. The breeding results of Standfuss, who backcrossed other moths for several generations, show exactly this phenomenon—the same type of hybrid constantly produced in every generation.

A similar behavior of the chromosomes has been recently described by Doncaster in a cross between other species of moths, and is illustrated in the following figures. The full number of chromosomes in the moth Biston hirtaria is shown in Fig. 48, *a*. There are 28 in all, of which four are small. Another species, Biston zonaria, has something over a hundred very small chromosomes (Fig. 48, *b*). The reduced number of chromosomes of the former species is 13 (one large one being coupled with a small one), of the latter 56. The chromosome group of the hybrid (zonaria ♀ by hirtaria ♂) is shown in Fig. 48, *c*. The exact number of chromosomes is difficult to count, but there are 14 large ones and about 56 small ones. In this hybrid a stage is passed through that resembles the synapsis stage. When the chromosomes emerge from this stage (Fig. 48, *c'*), almost the full number are found present, although Doncaster thinks that a few of them have united in pairs; for as shown in the figure there are now 12 or 13 large and 50 or 51 small chromosomes. These are a few less than the full number present before synapsis. In this case, how-

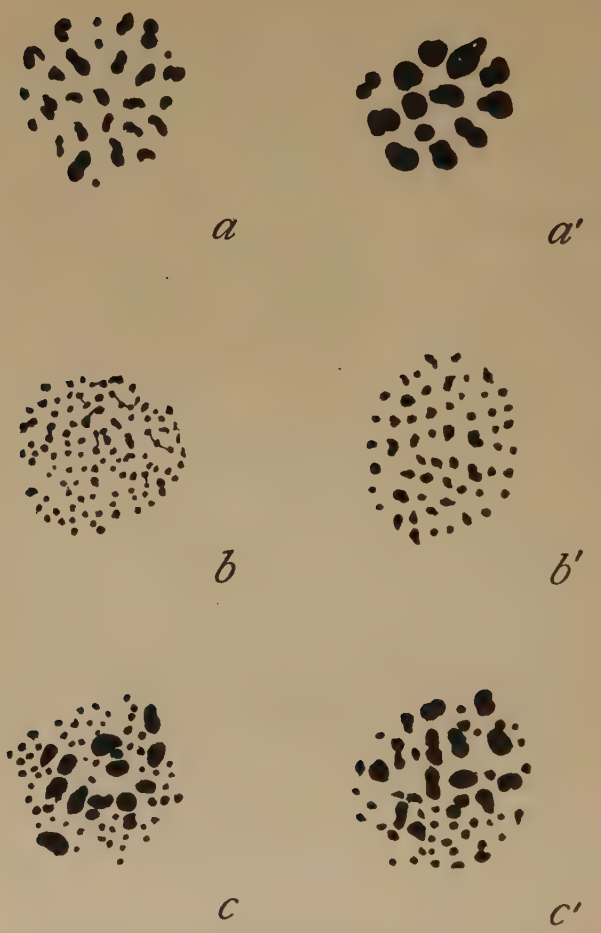


Fig. 48.—Biston hirtaria; *a*, spermatogonial chromosomes; *a′*, primary spermatocyte chromosomes (reduced number). Biston zonaria; *b*, spermatogonial chromosomes; *b′*, primary spermatocytes (reduced number). Hybrid, out of zonaria female by hirtaria male; *c*, spermatogonial chromosomes; *c′*, primary spermatocytes. (After Harrison and Doncaster.)

ever, no data concerning the genetic behavior of the hybrids have been reported.

Another instance of parallelism between unusual chromosome phenomena and genetic results is that found in Œnothera lata and semilata by Lutz, Gates and Thomas. The normal chromosome number in Œnothera lamarckiana is 14, but the race called lata always has 15 chromosomes, *i.e.*, one kind of chromosome exists in the triploid number. This is true even of lata plants which originated independently of the ordinary stock, in widely different races of Œnothera. The same results apply to semilata, which appears to be a variety of lata. Lata and semilata occasionally arise "spontaneously" from lamarckiana, in a small per cent. of the offspring of any one individual, and the explanation for this may be found in the fact that occasionally, in the gametogenesis of lamarckiana, two mated chromosomes, instead of separating, pass to the same pole (non-disjunction) so that the offspring would have three chromosomes of this type and contain 15 chromosomes in all. The behavior of the extra chromosome in the lata individuals is also of interest, for it is found that in gametogenesis, when the mated chromosomes separate, the extra chromosome does not divide regularly as do unpaired chromosomes in moths, but tends to pass to one pole. This would result in half the gametes containing it and transmitting the lata condition and the other half being normal. Very often, however, the chromosome lags on the spindle and so fails to be included in the nucleus of either daughter

cell, or it may even be torn apart, as if by spindle fibers from opposite poles. Consequently less than half of the gametes (at least the sperm, for gametogenesis was not studied in the female organs) receive the extra chromosome. The proportion varies greatly in different individuals. This conforms with the genetic result that lata individuals, crossed to lamarckiana, give varying proportions of lata offspring but never produce offspring more than half of which are lata.

In Primula, a striking case of correspondence between abnormal genetic and chromosome phenomena has been found, that appears strongly in favor of the chromosome hypothesis, although the discoverer, Gregory, has hesitated to draw this conclusion. Two giant races of the primula (P. sinensis) were found to have twice the number of chromosomes characteristic of other domesticated races. The breeding experiments with these plants show that they also have a double set of factors as compared with the same factors in ordinary primulas. While in ordinary plants the chromosomes are paired and, therefore, each factor is represented twice, for instance by A and A, in the giants there are four like-chromosomes, hence four factors AAAA. If the giant race contains some factors already mutated, such as A^1, the giant might contain one, two, three, or four of the mutant factors A^1. Such plants would be $AAAA^1$ or AAA^1A^1 or $AA^1A^1A^1$ or $A^1A^1A^1A^1$. As stated above, the breeding work shows that there is a double set of factors, but the evidence is as yet insufficient to de-

cide whether a mutant factor A^1 has as its mate, i.e. always pairs at maturation with, a special one of the remaining A's or may become the mate of any one of the three. On the chromosome hypothesis we should expect, on the whole, the latter to be true. Whichever of these views becomes established the parallel between the double set of chromosomes and the double set of factors is the important fact. Gregory admits this, but adds the caution: "Yet on the other hand the tetraploid number of chromosomes may be nothing more than an index of the quadruple nature of the cell as a whole."

In the preceding cases it has been shown that the factors and the chromosomes have the *same method* of distribution. In the case of sex and sex linked factors it can even be shown that they have the *same* distribution as the sex chromosomes. This identity of distribution holds not only for F_2 results and F_3 tests, but for all kinds of backcrosses as well. The relation holds, moreover, for all known sex linked factors, of which in Drosophila there are more than forty cases, and for all combinations of sex linked factors. Not to interpret this evidence to mean that the factors are contained in and carried by the chromosomes is to reject a mechanistic basis known to exist in the cell. Nothing is gained if, in order to avoid the obvious connection between the inheritance of the character and the transmission of the chromosome, we assume that something else in the cell, a portion of the cytoplasm, perhaps, also follows the distribution of the sex chromosomes. Such a postu-

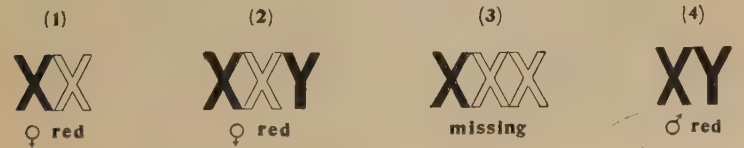
late only adds an unknown and improbable assumption and leaves the situation less clear than before.

The advantage of the chromosomal interpretation as applied to the sex chromosomes is nowhere better illustrated than in the history of a process called non-disjunction, which was discovered by Bridges. Furthermore this case, supported on the one hand by extensive and definite experimental breeding and on the other hand by cytological investigation, offers the most direct evidence yet obtained concerning the relations of particular characters and particular chromosomes, for in this case an abnormal distribution of the sex chromosomes goes hand in hand with an identical abnormal distribution of all sex linked factors. It was found that females from a certain strain of white-eyed flies gave, on out-crossing, about 5 per cent. of unexpected classes. For instance, one of the white females crossed to a red-eyed male (wild type) produced not only red-eyed daughters and white-eyed sons, as expected, but also a few white-eyed daughters and a corresponding number of red-eyed sons. The approximate percentage in which these classes appeared is as follows:

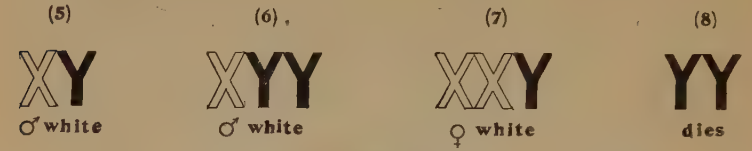
Red ♀	White ♂	White ♀	Red ♂
47.5%	47.5%	2.5%	2.5%

In general, therefore, there were 95 per cent. of expected forms and 5 per cent. of offspring that were apparently inconsistent with expectation on the chromosome theory. Closer inspection of these

results showed that the exceptions could be explained, if, occasionally, the two X chromosomes failed to disjoin in the reduction division, both passing out of some of the eggs of the white-eyed mother into the polar body, or, conversely, both remaining in the egg. If the two white-bearing X's should remain in the egg then such an egg fertilized by a Y sperm would give rise to a white-eyed daughter. Likewise the no-X egg fertilized by the X sperm of a red-eyed male would give a red-eyed son. The white daughters would, as just shown, contain two X's and one Y chromosome, unlike ordinary daughters, which contain two X's only. Since in these females there are three sex chromosomes instead of a pair, at the reduction division two must pass into one cell and one into the other. This division might take place in four ways: $\frac{XY}{X}$, $\frac{X}{XY}$, $\frac{Y}{XX}$ and $\frac{XX}{Y}$ (representing the egg below and the polar body above in each case). The first two types of reduction, depending on a more symmetrical pairing of the chromosomes, might be more frequent than the other two types. There would then be four types of eggs—a large number of X and XY eggs, and a few XX and Y eggs. Let us suppose that an XXY white female is mated to a red male. The progeny produced by the X bearing sperm would be:



The same series of eggs fertilized by the male-producing sperm, which carries a Y chromosome, would give:



If we consider these eight kinds of progeny we see that the exceptional white females (7) would be expected to repeat the process and be non-disjunctional. This is what actually occurs, for all white females that are the product of such a cross do, in fact, give non-disjunction in the next generation.

The red males (4) are an exceptional class but should not give exceptional results when bred to any normal female, nor should they transmit non-disjunction. This has been shown to be true.

The red females are not alike in composition, half of them (1) should behave like normal females heterozygous for white and the other half (2) should give exceptions. There are in fact found to be these two kinds of red females in equal numbers.

The white males (5) and (6) are not alike; one kind (5) is normal and the other (6) has two Y chromosomes. The latter should be expected to produce some XY sperm. These sperm would give daughters which would not be exceptions, but such females, with a formula XXY, should produce exceptions. In fact from half of the white males (5 and 6), daughters are produced that give non-disjunction.

The results bear out to a remarkable degree the hypothesis that they are due to a non-disjunction of the sex chromosomes caused by the presence of a Y chromosome in the females.

The hypothesis is capable of verification and Bridges has made a study of the chromosomes of the non-disjunctional females. He finds that such

FIG. 49.—Group of chromosomes of an XXY female of a non-disjunctional "line."

females contain an extra chromosome whose size, shape and position show it to be a supernumerary Y-chromosome. The normal group of chromosomes of the female of Drosophila ampelophila is shown in Fig. 12, and a group from a non-disjunction female in Fig. 49. They differ by one chromosome, namely, the extra Y.

One additional fact must be mentioned. If an XXY female should be fertilized by an XYY male

some females would be produced that are XXYY, owing to the union of an XY egg with an XY sperm or an XX egg with a YY sperm. One such female was found—she had two X and two Y chromosomes.

Here then is a case that seemed at first to be in direct contradiction to the scheme of sex linked inheritance based on the chromosome hypothesis, which proved, however, on further examination to give a brilliant confirmation of that theory; for not only can the hereditary results be accounted for, but the theory on which they were based was directly confirmed by a microscopical study of the chromosomes themselves.

Cases indicating non-disjunction have also been obtained in Abraxas, by Doncaster. As stated in the chapter on Sex Inheritance, he has found a strain in which the males have 56 chromosomes—the normal number, but the females have only 55 instead of 56 chromosomes. It seems reasonable, then, to suppose that such females arose by the passing of the two sex chromosomes, ZZ, to one pole (spermatocyte) leaving none at the other pole of the cell. The sperm resulting from the no-Z cell fertilizing a Z egg would give a ZO individual which would be a female with 55 chromosomes. All the daughters of the ZO female would be ZO and her sons ZZ individuals: and the race would continue in this fashion. On the other hand, if the ZZ sperm produced by non-disjunction fertilized a W egg, a male WZZ, corresponding to the XXY female of Drosophila, would be formed. Such a male would give rise to some sperm

carrying both Z and W, and if such a ZW sperm fertilized a zero egg of the 55 chromosome female, a 56 chromosome female would be produced. Doncaster actually found such a female among offspring from a cross of a female from the 55 chromosome race with wild type male, and he found also the genetic exceptions required on the assumption that this male was a WZZ form.

CHAPTER VIII

MULTIPLE ALLELOMORPHS

The meaning of the term multiple allelomorphs may be illustrated by the following example:

1. If a white-eyed male of Drosophila is mated to a red-eyed female, the F_2 ratio of 3 reds to 1 white is explained by Mendel's law, on the basis that the factor for red is the allelomorph of the factor for white.

2. If an eosin-eyed male is mated to a red-eyed female, the F_2 ratio of 3 reds to 1 eosin is also explained if eosin and red are allelomorphs.

3. If the same white-eyed male is bred to an eosin-eyed female, the F_2 ratio of 3 eosins to 1 white is again explained by making eosin and white allelomorphs.

There are here three factors, any two of which may meet, and whenever they do, they behave as allelomorphs. They form a system of triple allelomorphs.

On the chromosome hypothesis the explanation of this relation is apparent. A mutant factor is located at a definite point in a particular chromosome; its normal allelomorph is supposed to occupy a corresponding position (locus) in the homologous chromosome. If another mutation occurs at the same place,

the new factor must act as an allelomorph to the first mutant, as well as to the "parent" normal allelomorph.

Since these factors have the same location they must all give the same linkage values with other factors. This has been shown to be true. For instance, the factor for white eye color of Drosophila is very closely linked to that for yellow body color. The "distance" between them is 1 unit, which means that crossing over takes place about once in a hundred times. Eosin eye color gives the same crossing over frequency with yellow.

White eye color gives with miniature wings about 33 per cent. crossing over. Eosin gives the same value with miniature.

White gives 44 per cent. of crossing over with bar eye. Eosin has the same value. Similar relations hold for all of the characters of the first group; they all have the same linkage values for eosin that they have for white. This example indicates that the conception of allelomorphs should not be limited to two different factors that occupy identical loci in homologous chromosomes, but that there may be three, as above, or even more different factors that stand in such a relation to each other. Since they lie in identical loci they are mutually exclusive, and therefore no more than two can occur in the same animal at the same time. This is both demonstrated by the facts and postulated by the chromosomal mechanism.

On *a priori* grounds also it is reasonable to suppose

that a factor could change in more than one way, and thus give rise to multiple allelomorphs, unless it is supposed that the only change possible in a factor is a complete loss of the factor, as postulated in the presence and absence theory.

There is, however, an alternative theory to that of multiple allelomorphism. This alternative is complete linkage. The numerical result can be equally well explained if, instead of occupying identical loci, the factors are so near together that they never (or very rarely) cross over. For reasons that will be given later we are inclined to think that the explanation of multiple allelomorphism is in most cases the more probable one, but the arguments in favor of this view may be deferred until the facts have been described.

There is a general relation that so far holds for all cases in which multiple allelomorphs have been discovered, namely, that the factor-differences produce similar effects. All of the following examples illustrate this relation.

In rabbits (Fig. 50) the Himalayan pattern has been shown to behave as a recessive to self-color and a dominant to albino. Any two of these three types of pigment formation and distribution give a 3:1 ratio in F_2 but no two of them, when crossed, ever produce the third genetic type. In other words the factors behave as though allelomorphic, for only two can be gotten into any one individual. A similar relation has been described by Baur in the columbine, where three types of leaves, green, variegated (green

FIG. 50.—Himalayan, black and white rabbits. The factor that stands for each is allelomorphic to the others.

and yellow), and yellow form a triple system. Emerson's case for pod and leaves in beans—green pods, green leaves; yellow pods, yellow leaves; yellow pods, green leaves—also fulfill the conditions of a triple allelomorph system. Shull has reported a case in Lychnis which he interprets as due to triple allelomorphs for sex-determining factors. Two of them give reversible mutations as have white and eosin in Drosophila.

Cases in which more than three allelomorphs have been found may next be considered. The cases seem to show that here also the same character is affected by each of the mutant factors that form the multiple system. In a few instances the characters have been recognized as due to multiple allelomorphs, but in most of them no sufficient interpretation has been offered or else the explanation of complete linkage has been advanced.

Tanaka has reported a case in the silkworm moth which seems best interpreted as one of quadruple allelomorphs. The four larval patterns called striped, moricaud, normal, and plain (Fig. 51), are the characters involved. Besides showing the ordinary behavior of multiple allelomorphs when mated together these characters show linkage to another pair of factors (for yellow and white cocoon color). So far as the data go, the strength of this linkage seems to be the same in all combinations tested.

In mice it has been shown (Cuénot, Morgan, Sturtevant, and Little) that yellow, black, gray with gray belly (wild type), and gray with white belly

(second wild type) are allelomorphs. It will be observed here that the factor in the wild type gray mouse is responsible for the appearance in each hair of the three pigments, chocolate, yellow and

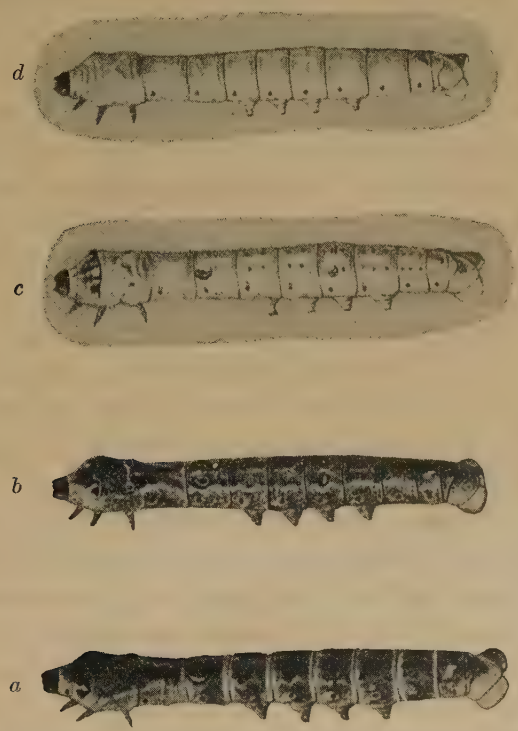


FIG. 51.—Four allelomorphic characters in the silkworm: *a*, Chinese striped yellow; *b*, Chinese moricaud yellow; *c*, Japanese normal yellow; *d*, Chinese plain white.

black. Gray is therefore a mosaic effect, for these colors are stratified in each hair from the base outward in the order above named. The allelomorphic factor for yellow gives rise to only one of these

colors, although the others may to some extent appear, especially in old mice. The third allelomorph produces only black or at least the chocolate pigment, if present, is obscured by the darker color. Finally, the fourth allelomorph produces gray on the back and sides while the belly is pure white (the under hair is black). This series illustrates how allelomorphs of the same locus may not only determine the color, but also act to determine where a color is to develop. The allelomorphs differ therefore in regard to what part of the body they affect, or the time in ontogeny when they act, as in the banded hair of the gray mouse.

This case serves, therefore, as an excellent introduction to the cases that Emerson has described in corn (maize), in which the red color of the grain (pericarp), cob, silk, and husk furnish a wonderful series of character combinations that can be explained on the multiple allelomorph hypothesis. Emerson adopted the hypothesis of complete linkage, but the same arguments as used in other cases lead us to prefer the alternative of multiple allelomorphs. In some varieties of corn the grain, cob, silk, and husk are all red; in others all white; in others the grain is red or variegated, the cob, silk, and husk white; in others the grain is white or variegated, and the rest red. Many different combinations are known, and so far as tested the combinations that go in through the two parents come out in F_2 according to expectation, *i.e.*, they give no new gametic recombinations. If we assume that there is a system of allelomorphs,

such that one affects one combination of parts, another a different combination, the results find a simple and consistent explanation. It may seem strange at first that a factor may make the cob red and not color the grain or husk, while another allelomorph may make the grain and husk red but not affect the cob color, but it is no more strange than that one factor determines one distribution of the pigment over the coat and even in each hair of the gray mouse and another one determines another distribution.

Equally striking is the series of forms of the grouse locust (Paratettix) that Nabours has recently studied. Nine true breeding forms that are found in nature were studied. They differ markedly in color pattern (Fig. 52) but each color pattern behaves as a unit in heredity. The hybrid is in a sense intermediate, the color characters of each parent being superimposed. In fact Nabours finds that simple inspection of the hybrid suffices to show which forms were its parents. In the germ cells of the hybrid the two parental color types segregate as units. The resulting F_2 types are in the 1 : 2 : 1 ratio. It is obvious, since only two of the color types can exist in the same individual, and since they separate in the germ cells, that the condition of multiple allelomorphism is fulfilled.

All Nabour's crosses relating to color pattern (with some possible exceptions) follow the plan just outlined. The case at first sight appears unique in that the color pattern of each type is complex in the sense that different parts of the body are differently affected

and in that in most cases the hybrid shows at the same time the characters of each parent. Both of these peculiarities occur in other cases, however,

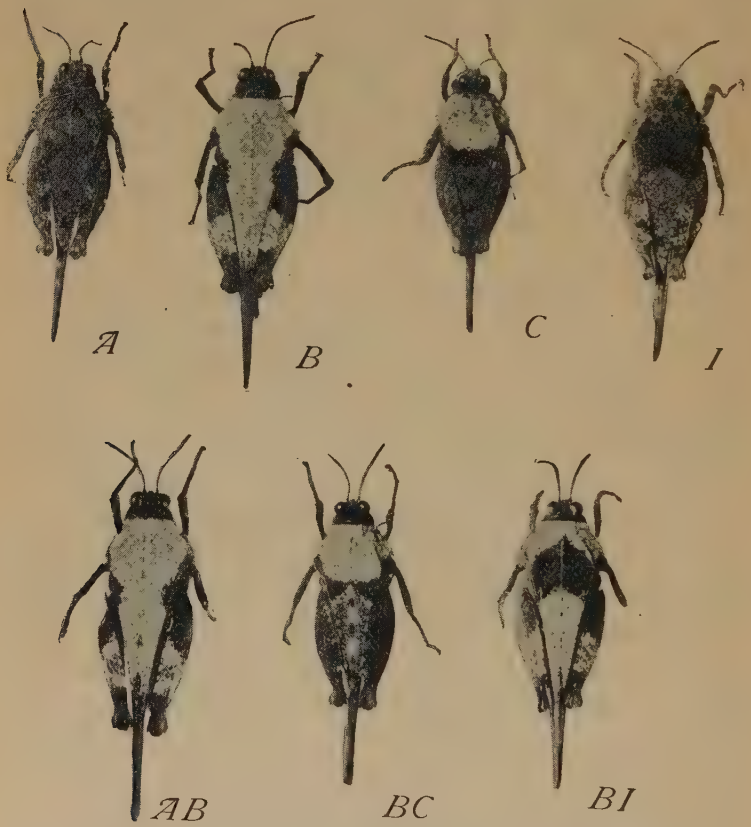


FIG. 52.—Four types, *A*, *B*, *C*, *I*, of Paratettix. Below are hybrids between *A* and *B*, *B* and *C*, and *B* and *I*. (After Nabours.)

as in Emerson's corn for instance, although nowhere perhaps so strikingly as in Paratettix.

In any attempt to decide between the two alter-

native views of identical loci and of complete linkage the method of origin of the mutant allelomorph is a matter of prime importance. Emerson has described one type ("variegated" corn) in which a mutation (to red) occurs frequently. This mutation is of such a sort, as Emerson points out, that, on the theory of complete linkage, it must involve the mutation of two factors at the same time. On the theory of multiple allelomorphs only one mutation is necessary each time the change occurs. Fortunately we have complete information concerning the origin of the types of Drosophila that fall into this category. One of these may now be given in detail before attempting to decide between the claims of the rival explanations.

In 1911 a few males with white eyes arose in a culture of red eyed flies. From them the stock of white eyed flies was obtained by the usual procedure. In 1912, in a culture of white eyed flies having also miniature wings and black body color, a male appeared that had eosin eyes. He also had miniature wings and black body color, so that there could be no question of his origin from this particular stock. The eosin stock is descended from this male.

In 1913, in a cross between vermilion eyed flies and wild flies several males appeared in F_2 whose eyes were quite different from vermilion. Analysis of the case showed that a mutation had taken place in the stock having vermilion eye color. The new color proved to be a double recessive, for vermilion and for a color called cherry. The new mutation had

not occurred at the locus of the vermilion factor, however, but at another locus where there had been a normal factor. Subsequent work with the cherry eye color showed that it was allelomorphic to white and to eosin, the three eye colors and their normal allelomorph forming a quadruple system.

To the preceding history must be added cases of the return mutation from eosin to white. Such a mutation occurred in 1914 in a culture of eosin flies with miniature wings. The parents had been treated with alcohol, but there is no evidence to show that the alcohol had any connection with the event. A single white eyed male appeared among many hundred eosin brothers and sisters. The male had miniature wings. When crossed by ordinary white it produced white through two generations. There can be little doubt that it is the same white as the original white. In a pure bred stock, eosin tan vermilion, a few males were found which had a white eye color instead of the cream color of eosin vermilion. These flies mated to white stock gave white offspring for two generations. Here the case was checked by two control characters, for the new white-eyed males showed tan body color and were proved to carry vermilion. In these controlled cases the mutation took place in the reverse direction from the original one. Three other cases of eosin returning to white which are apparently not explainable by contamination are also recorded.

The appearance of eosin in the white-eyed stock

might be interpreted to mean that a mutation in eye color had appeared in the white-eyed stock in a factor located near the factor for white ("completely linked" with it) and that the effect of this new factor, combined with that of the factor for white, which was already there, gave the color that we call eosin. Eosin from this point of view would be due to two consecutive mutations of completely linked, neighboring loci. This interpretation of two consecutive mutations can not be made in the case of cherry, however, for cherry arose from red by one step, just as did white; yet cherry, like eosin, when mated to white, does not give rise to offspring that are red. It would follow on the complete linkage view that cherry and white differ from red by the same factor, but since they are not alike, that one of them must differ from red by still another factor. Since each arose from red immediately, it would follow that one of them must have arisen by a simultaneous mutation in two factors completely linked and affecting the same character. All these assumptions must be made on the theory of complete linkage, but are avoided on the alternative theory of multiple allelomorphs.

Exactly the same argument applies to many of the other multiple allelomorph systems of Drosophila. The recessive mutants pink and peach-colored eyes each arose independently from red eyed flies, yet when crossed do not give red, but a color intermediate between pink and peach. Secondly, sooty body color arose in wild stock, although it was found only

after the stock had been crossed to ebony, with which it is allelomorphic. Here too the mutant forms though both recessive to normal do not give normal gray color when crossed together, but a color intermediate between sooty and ebony. In both of these cases the complete linkage view would require that one of the mutant types had originated by a mutation in two factors at once. In the case of another set

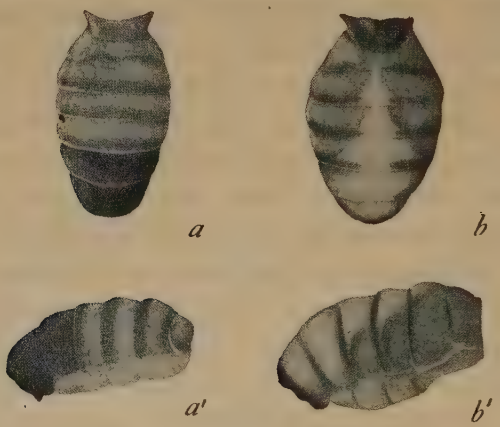


FIG. 53.—The abdomen of normal a,a , and spot, b,b', males. The other allelomorph is yellow (not shown here).

of triple allelomorphs known in Drosophila, namely, yellow and spot (Fig. 53) and their normal allelomorph. The above argument does not apply; for although spot and yellow are both recessive to gray and give yellow when crossed to each other, spot originated in flies already containing the allelomorph for yellow.

The reasons may now be given that incline us to think that the theory of identical loci is much more

probable for the cases known than is that of complete linkage (in the sense defined). No one of the reasons is in itself conclusive, but taken together they weight the scales heavily on one side.

1. When two mutants that depend on "multiple allelomorphs" are crossed they give in F_1 a type that is like one or the other of the two mutants, or an intermediate type. This type is scarcely ever like the original (or wild) type. In this respect they differ from other recessive mutant types which when crossed together give the wild type. We understand why in the latter cases the wild form is recovered. It is because each mutant type contains besides its mutant factor the normal (dominant) allelomorph of the other type. Hence the original type is reconstituted in the cross, as has been already stated. But when two mutant allelomorphs occupying the same locus are brought together neither of them brings in the normal allelomorph of the other; hence the wild type is not reconstituted. If the cases in which these allelomorphic factors arose independently are not cases of identical loci then the explanation involves the occurrence of two mutations at the same time, as explained in the case of cherry.

2. It is a characteristic of "multiple allelomorphs" that the same character is affected. Nearness of factors in the chromosome will not explain this fact unless nearness means the same factorial basis, for in the other mutants that we have obtained, nearness of factors is in no way related to the kind of character

or part of the body that is affected. It seems therefore more probable that this peculiar fact connected with multiple allelomorphs means that the same portion of the chromosome is changed in one or another direction.

3. It is true that a very wide range of linkage values has been obtained, that extends from almost free segregation to less than 1 per cent. of crossovers. However, if we should construct a curve showing the number of cases exhibiting the various possible linkage values, the number showing complete linkage or, as we should say, multiple allelomorphism, would be far in excess of the number of these to be expected from the general shape of the rest of the curve. This indicates that multiple allelomorphs are in a class by themselves, not merely extreme cases of the same type as an ordinary linkage case.

4. There is an *a priori* consideration that may not be out of place in the argument. There is no sufficient reason for supposing that only one sort of mutation can occur in a given locus in the chromosome. If the basis of the chromosome is a chain of chemically complex substances (*e.g.*, proteins), any slight addition or loss or even re-arrangement of the atoms in the molecules of a bead in such a chain might well produce an effect on the organism, and perhaps a more marked effect on that particular character that stands in closest relation to that chemical body. Since we know that mutations and even "reverse" mutations actually occur, it would be indeed strange if only one kind of change were

possible in a given locus. But if more than one kind of change did take place in a locus, a series of multiple allelomorphs would result.

The ability of the theory of multiple allelomorphs (identical loci) to explain the peculiarities of so many cases in such widely separated fields proves the usefulness of the hypothesis. Although the theory of complete linkage also will cover the numerical results in these cases (and some of the simpler cases cited may prove to fall under this head) there is the very strong first-hand evidence that has just been given that makes the theory of multiple allelomorphs more probable than the former theory. It is important to recognize that there is this strong evidence in favor of multiple allelomorphs, quite aside from special cases of complete linkage, for, as will be shown in the next chapter, there are some far-reaching consequences of the theory of multiple allelomorphs.

A word may not be out of place here concerning the relation of the theory of multiple allelomorphs to the question of the variability of factors. The fact that more than one change may take place in the material at a given locus must not be taken to mean that the material is undergoing continuous fluctuation, for such mutations occur rarely and afterward behave as do other mutations. In only one well established case, that of variegated corn, do mutations appear frequently at a given locus. But even in such a case the change can not properly be said to be fluctuating, but is of a fixed nature, and when it has once occurred the new factor

is no more subject to mutation than are other factors, *i.e.*, the factor has lost its unusual instability.

There is no *a priori* answer possible to the question as to whether a mutation having occurred, a further mutation of the mutated factor is more likely to occur, for it is conceivable that while in one case the new factor might be unstable, in another case it might be even more stable than the original one. In regard to the other question, as to whether a particular locus is more liable to mutate, the work on Drosophila shows that certain loci do mutate more often than do others, and this is shown not only in the recurrence of the same mutation, but also in the occurrence of multiple allelomorphs.

At present the series of white allelomorphs is: white, eosin, cherry, blood, tinged, buff, ecru, ivory, coral, and apricot. Each of these forms has appeared by direct mutation from the wild-type. Crossed to each other, the members of this series give compounds that are intermediate in color between the two types used as parents. In no case do such crosses give wild-type progeny, which would be the result expected if they were closely linked but non-allelomorphic mutants. The hypothesis of close linkage would require here the absurd supposition that each type was produced not simply by one change but by as many simultaneous changes as there are mutant types in the series.

CHAPTER IX

MULTIPLE FACTORS

The term "multiple factors" has come, in practice, to be applied usually to cases in which two or more factor-differences occur, all of which produce similar effects. The frequency with which such cases are found is not surprising, since, on the factorial interpretation of heredity, it is apparent that many factors must contribute toward the making of every character. For example, the character, eye color, can appear only after the complex series of developmental reactions has taken place, whereby in turn head, eyes, pigment cells, etc., have been formed, and so this character must ultimately depend on all the factors affecting these processes. There must, besides, be many factors that operate in a more direct manner in the production of nearly every character, since on analysis even the simplest character usually proves to be the resultant of many components, both physical and chemical. Thus the color of the eye must depend, among other things, on the size of the pigment granules, on their number and on their color, and the color of the pigment may in turn be dependent on reactions in which many substances take part. It is therefore evident that an apparently simple character, like eye

color, involving only one organ, is, so far as its mode of inheritance is concerned, in no wise different in kind from a complex character like stature which, as Bateson pointed out in 1902, must depend on all factors affecting length of head, neck, trunk, or legs.

In the case of eye color in Drosophila, more than 25 factor-differences have arisen by mutation. Most of these factor-differences are dissimilar in their effects upon the eye color—thus, one differentiates a purple eyed fly from the red, another differentiates vermilion from red, another white from red, and so on. It so happens, however, that two mutations occurred, one in the sex-linked group, and one in the third, each of which changed the red eye to a pink color. It is to such cases only—where factor-differences produce the same or very similar effects, or effects that differ only in degree—that the term "multiple factors" has come to be specifically applied. It should be recognized that this restriction of the term is arbitrary, but there is a practical advantage in grouping these particular cases together under a common heading, because crosses involving several factor-differences that are similar in effect give peculiar ratios and present certain difficulties to a factorial analysis, not commonly met with elsewhere.

In the above illustration of the sex-linked and third chromosome pinks the two factor-differences were not present in the same cross, and their inheritance was worked out separately. They were shown to be in different loci, not by their behavior

with reference to each other, but by their different linkage values with other factors.

An example of a cross, involving at the same time two factor-differences which have similar effects, is Nilsson-Ehle's cross of dark brown oats having two dominant factors for dark glumes with white-glumed plants having the two recessive allelomorphic factors for light color. The expected F_2 ratio is 9 double dominant dark browns (AB): 3 light browns having the first recessive and the second dominant (aB): 3 light browns having the first dominant and the second recessive (Ab): 1 double recessive white (ab). Since the two factor-differences produce similar results, however, the light browns, aB and Ab, are indistinguishable; counting these two classes together, a 9:6:1 ratio results. The 9 double dominants were distinguishable from the 6 single dominants, the pigment being dark brown in the 9 cases where both factors for dark glumes were present and both factors for light glumes absent, but only light brown in the 6 cases where one light and one dark factor were present. Similarly the 1 double recessive, having both light and no dark factors, was much lighter even than the 6 light browns. This result may be *described* by saying that the effects of the factors for dark and for light were all *cumulative* or summative, two darks producing a blacker pigment than one, and two lights a paler color than one.

In many cases, multiple factors do not give results that may, in the above sense, be called cumulative. For example, if a white-flowered sweet pea (ab)

having two pairs of recessive factors for white is crossed with a colored sweet pea (AB), it is found when the 9AB: 3aB: 3Ab: 1ab individuals appear in F_2 that the aB and Ab plants, having only one factor for white and one for red, are just as white as the ab plants. In other words, the ab class can show no cumulative effect of the two white factors. Since the three latter classes all look white, they are added together in the count, and a ratio of 9 reds : 7 whites results.

It is commonly said that this result is due to the occurrence of two factors "for red" (the dominants, A and B), neither of which alone is sufficient to produce any effect (since Ab and aB look no different from ab), but which, when present together, act as *complements* to each other and thus produce the red color. Such an interpretation fails, however, to take into consideration the possible effects of the recessive factors "for white" (a and b). It is therefore unwarranted, unless the "presence and absence" view be accepted, namely, that the dominants are the only real factors, the recessives being mere absences. It would likewise be unwarranted, of course, to ascribe the results purely to the recessive factors, and so to conclude the similarity of aB and Ab to ab was due to the fact that a and b were non-cumulative in their effects. Neither of these methods of describing such cases is therefore to be regarded as more than a shorthand statement of the empirical facts.

In the cross of Bursa which follows, Shull, using the presence and absence scheme, treated the case

as one of two similar dominant factors producing a non-cumulative result. (Here, then, the 9AB resemble the 3aB and 3Ab individuals and a 15:1 ratio results.) To those who reject the idea that dominance implies presence, recessiveness absence, there is no great distinction between this case and that of

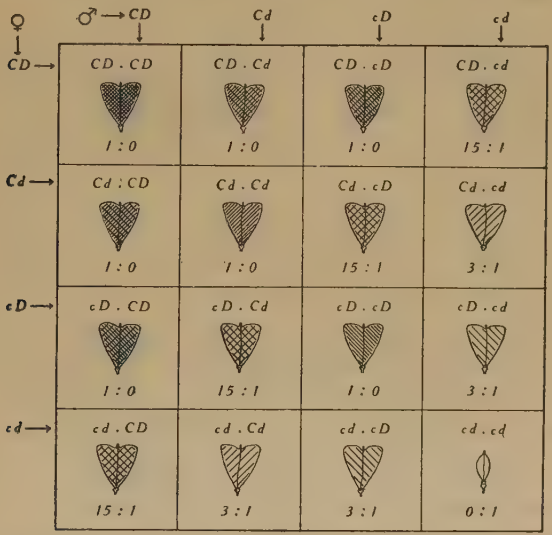


FIG. 54.—Diagram showing the kinds and composition of the F_2 capsules of Bursa bursa-pastoris. (After Shull.)

the two whites with a 9:7 ratio. Shull found that when a plant of Bursa bursa-pastoris with round capsules is crossed to one with triangular capsules, the round is recessive to triangular in F_1. In F_2 the round reappears only once in sixteen times (Fig. 54). Thus in this cross round may be treated as the resultant of the two recessive factors, either of which by

itself does not change the triangular type, as shown by the fact that both single recessives are triangular in type and are identical in appearance with the double dominant. Only where the two recessives occur in the same individual does the type change to round.

Six families were bred from the F_1, and gave the following counts:

	Triangular	Round	Ratio
	507	30	16.9 : 1
	146	4	36.5 : 1
	48	3	16.1 : 1
	179	9	19.9 : 1
	1743	72	24.2 : 1
	159	7	22.7 : 1
Totals	2782	125	22.3 : 1
Expected	2725	182	15.0 : 1

The actual ratios range from 16 : 1 to 36.5 : 1, which exceed the expected ratio of 15 : 1. Nevertheless, the deficiency in the round class is probably due to the lower viability of the round-capsuled type, for in later cultures where the conditions were more favorable the expected 15 : 1 ratios are more nearly realized. That 15 : 1 is the true ratio is shown by tests that were applied to these F_2 plants. In Fig. 54, the 16 classes (15 : 1) of F_2 individuals are represented. Within each square is also given the genetic composition of the class. The letter "c" stands for one of the recessive factors, and the letter "d" for the other factor. Both of these recessive factors acting in conjunction produce the round capsules ccdd. Beneath each figure is given the expected ratio for

the next generation when the plant of that composition is self-fertilized. It will be observed that the

1 : 0 ratio is expected 7 times.
3 : 1 ratio is expected 4 times.
15 : 1 ratio is expected 4 times.
0 : 1 ratio is expected 1 time.

This test was applied by Shull to his F_2 plants of the triangular type. There were seven families that gave a 1 : 0 ratio, four that gave approximately a 3 : 1 ratio, and six that gave a 15 : 1 ratio. These results are in fair accord with the expected numbers given above.

When a further test was carried out by breeding from the six 15 : 1 families of the F_3 group above (which should be expected to give the same results as the F_2 class, because they have the same composition), the ratios obtained were as follows:

1 : 0 ratio expected 35; realized 39.
3 : 1 ratio expected 20; realized 12.
15 : 1 ratio expected 20; realized 26.

The results agree again fairly well with the expectation.

A second test is found in self-fertilizing plants from families that gave a 3 : 1 ratio. As the diagram shows these contain only the one ("c") or the other ("d") factor, they should give only homogeneous families and 3 : 1 families—never 15 : 1 families. This result also was obtained.

Nilsson-Ehle found that three recessive factors must combine to produce an effect which, in the

following case, is the production of a white-seeded wheat. A cross between white-seeded and red-seeded wheat gave in F_2 one white to sixty-three reds, showing that three independent recessive factors were involved.

Nilsson-Ehle also found that in oats a type without ligules reappeared in F_2 in such a ratio that four recessive factors must have combined to have produced the type without ligules. East found certain kinds of yellow corn that gave in F_2 fifteen yellows to one white. We may here also interpret the white as the double recessive. East has pointed out that in crosses of certain strains of red corn white appears in F_2 in such a way as to suggest that three or possibly four recessive factors combine to produce white.

In other cases of multiple factors, the two factor-differences differ in the intensity of their effect, and so in F_2 the two classes aB and Ab can be distinguished from each other, and a 9:3:3:1 ratio therefore results. In some of these cases, however, the factors are in a sense non-cumulative in that one of the factor-differences produces no effect when a given allelomorph of the other pair of factors is present. Thus, in the ratio 9AB:3aB:3Ab:1ab if, in the presence of b, a and A produce no different effect there would be a ratio of 9:3:4. This is true in a cross of a black mouse (AB) with a white mouse carrying both the recessive factor (b) for producing an absolutely white color and also the recessive (a) which merely "dilutes" the black to blue. The "diluter" a of course can not have any visible effect

in a mouse already carrying b and therefore white. There are also reverse cases where, in the presence of B, a and A produce no different effect and thus a ratio of 12AB + aB:3Ab:1ab is obtained.

Departures from the 9:3:3:1 ratio different from those given above result if one factor for a character is dominant and another recessive. For example, there is a white race of fowls that is dominant and another white race that is recessive. There are two cocoon colors in silkworm moths that have this same relation. A cross of a dominant white to a recessive white gives a ratio of 13:3. Here, instead of the recessive classes resembling each other, so that a 9:6:1 or 9:7 ratio is produced, both the 9AB and 3Ab, since they contain the dominant white (A), resemble the one ab containing the recessive white (b), and only the 3aB appear colored. In this case the effect of the white does not happen to be cumulative, but there is no reason why factors which differ as to dominance should not have a cumulative action; if they did, a 3:10:3 ratio would result.

Cases belonging to any of the types above show ratios further modified if dominance is incomplete, for then the heterozygous classes are intermediate in character between the others. Consequently, in these cases, the different classes are usually not as easy to distinguish from one another as if dominance were complete, for the character differences now separating the classes are smaller. In such cases, especially if the character is appreciably influenced by environmental conditions, the individuals in any

one class may vary so much from each other as to overstep the small differences separating the classes. An accurate separation of the individuals into different classes and a count of the number in each class is then impossible, and it becomes so difficult to determine the number of factors involved and the effect of each factor (or, rather, factor-difference) that such cases have at times been used in attempts to disprove the factorial hypothesis. The problem is likewise more difficult if more than two factor-differences occur. This is true especially in those cases where the effects of the different factors are cumulative, for then classes are produced showing characters intermediate in various degrees between the characters of the most extreme classes, just as in cases of incomplete dominance. It will be instructive to consider several instances of crosses of the above types, since, although definite ratios can not be obtained, there are various characteristic effects produced which show that multiple factors are responsible for the peculiarities of the results.

The inheritance of black color in Drosophila has already been described. Black is recessive to the normal ("gray") color, but the heterozygous forms are a little darker than the pure grays. Ebony is another body color, similar in appearance to black, but somewhat darker. It is similarly recessive to gray, but the factor responsible for it is located in a different chromosome (III) from that which carries the factor for black (II). When black and ebony are mated together we should expect gray flies in F_1.

Such flies were actually obtained, although they were rather dark in color, since both black and ebony produce some effects on flies heterozygous for them. In F_2 the expectation is 9 gray, 3 black, 3 ebony, and 1 black ebony (double recessive). When F_2 was actually obtained it was found to be impossible to make an accurate separation of the four classes. There was a practically complete series ranging from the normal gray to individuals darker than either black or ebony. The gradation is obviously due chiefly to the fact that dominance is not complete. There are nine different classes expected, instead of four, if heterozygous forms be counted. These nine classes form groups, each with its own mode, the outlying members of each group overlapping neighboring groups. To add to the difficulty, the colors change considerably with the age of the fly. There are at least seven other mutant factors known in Drosophila that make the flies darker. It will readily be seen that, if one had a population containing a mixture of all these characters, analysis would be well-nigh impossible.

Before making the above cross the inheritance of black and of ebony had been studied separately, and no difficulty in classification is encountered unless they are used in the same cross. This information made it possible for us to interpret the black ebony cross. In the experiments now to be described, we are dealing with factors which had not first been studied separately, so that the interpretation is not so obvious as in the preceding case.

Two varieties of tobacco, Nicotiana alata grandiflora and N. forgetiana, were crossed by East. They differ mainly in the size and color of the flower. The corolla is three times as long in one as in the other variety, as seen in Fig. 55. In the table, page 185, the lengths of the corolla in the two varieties,

FIG. 55.—At the left a flower of Nicotiana alata grandiflora; at the right a flower of N. forgetiana; in the middle the F_1 hybrid. (After East.)

in the F_1, and in the F_2 plants are given. The table shows the small *variability* of the parents. The F_1 generation is intermediate in length and also shows little variability, while the F_2 generation gives no definite ratios but exhibits great variability (Fig. 56), and overlaps the two grandparental types, although only a few flowers in F_2 are identical in size with those of each of the two grandparental types. These results are those expected if the two parent varieties

differ in several factors that affect their size. If the parent strains were pure the F_1 hybrids would all be alike, or rather would show little if any more variability than either parent stock, because all these F_1 plants receive the same contributions from the

FIG. 56.—At left, a flower of Nicotiana alata grandiflora; at right N. forgetiana; between them are four F_2 flowers, showing the result of segregation both in the length and the spread of the corolla. (After East.)

parents. But when in the gametogenesis of the F_1 plants these factors segregate, many new combinations will be formed, and among them will be a few combinations like those in the original varieties; hence we expect in the F_2 a wider variability, with a return to the grandparental types in a certain percentage of the plants. East suggests that four pairs of factors may cover the results in this instance.

FREQUENCY DISTRIBUTIONS FOR LENGTH OF COROLLA IN A CROSS BETWEEN NICOTIANA FORGETIANA AND N. ALATA GRANDIFLORA. EAST

Designation	Class centers in millimeters														
	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90
N. forgetiana, 314	9	133	28												
N. alata gr., 321										1	19	50	56	32	9
F_1 (314 × 321)				3	30	58	20								
F_2 (314 × 321)1−6		5	27	79	136	125	132	102	105	64	30	15	6	2	

CLASSIFICATION IN RELATION TO PARENTS BASED ON SKULL LENGTHS AND ULNA LENGTHS, TO SHOW THE RELATIVE VARIABILITY OF THE TWO MEASUREMENTS AND OF THE FIRST GENERATION (F_1) AND THE BACKCROSS (B.C.). MACDOWELL

Character	Generation	−13	−12	−11	−10	−9	−8	−7	−6	−5	−4	−3	−2	−1	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25
Length of skull	F_1																					2	2	8	5	10	7	3	2	2										
	B.C.													3	6	4	13	18	42	32	38	34	16	16	8	4	3	1												
Length of ulna	F_1													1		1			2		1	1	1	2	2	5	3	1	7	3	2	1				2		1		1
	B.C.						1		2	3	1	2	4	4	12	11	20	26	17	19	18	15	12	13	15	11	5	2	4	2	2			1	1					

A race of pigeons called fantails differs from other pigeons, and from birds in general, by the large number of feathers in the tail. The ordinary pigeons have

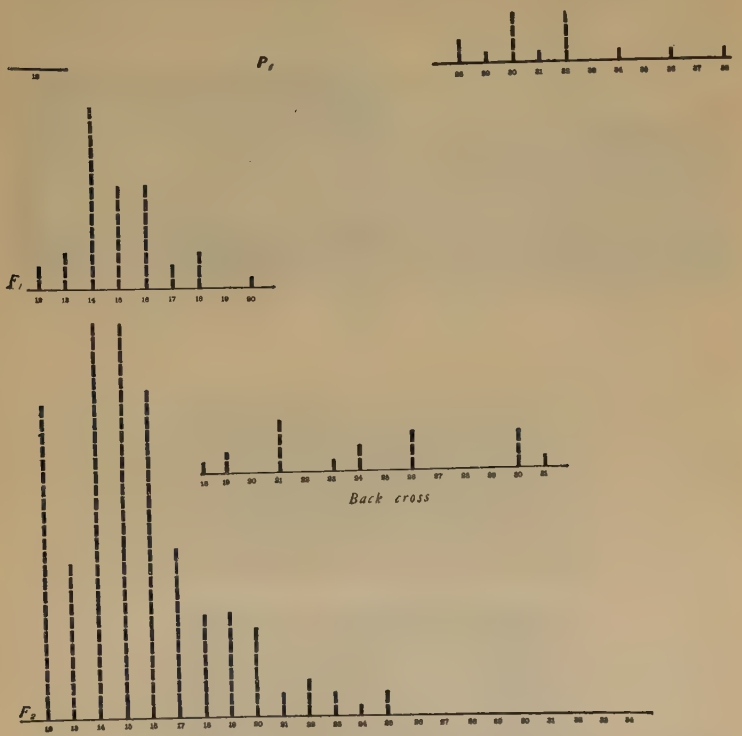


FIG. 57.—Illustrating the results of a cross between pigeons with 12 tail feathers and a race of fantail pigeons with from 28 to 38 tail feathers. The number of feathers in P_1, F_1, F_2, and the offspring of the backcross (F_1 by fan tail) is given. In each case the numbers on the base line stand for tail feathers. The vertical rows are the classes.

twelve tail feathers; the fantails used in the cross have from 28 to 38 tail feathers. The F_1 hybrids (41 birds) have from 12 to 20 tail feathers; the F_2 have 12 to 25 in a count of 67 birds. When the F_1

birds are backcrossed (Fig. 57) to the fantail the number of feathers varies from 19 to 31. On the hypothesis that the race of fantails has been built up by the accumulation of several factors these results can be understood.

MacDowell has compared the length of skull and of one of the bones in the leg (ulna) of hybrids between domesticated races of rabbits in the F_1 generation and in the backcross. As shown in the table, page 185, the variability of the backcross is in both characters greater than that of F_1. Similar though less convincing evidence was obtained for body weight also.

The inheritance of ear length in rabbits has been studied by Castle in a cross between lop-eared and short-eared races (Fig. 58). He shows that the F_1 generation has ears of intermediate length and that the blend is "permanent," *i.e.*, that "no reappearance of the grandparental ear length occurs in generation F_2, nor are the individuals of the second generation, as a rule, more variable than those of the first generation of cross breeds." In the light of MacDowell's results for other quantitative characters in rabbits it seems more probable that the number of factors involved is greater for ear length than in the other cases, hence more data will be necessary before we can be certain that no reappearance of the grandparental types will be found in F_2. If four independent factors were involved either grandparental type would be expected to reappear only once in 256 times, with six factors only once in 4096

times, etc. It would require a large number of offspring to prove the multiple factor hypothesis if the reappearance of the grandparental types be demanded for such a proof.

FIG. 58.—Short-eared by lop-eared rabbit. F_1, son of last; F_2, daughter of F_1 by his sister. (After Castle.)

Several excellent cases of multiple factors have been worked out with Indian corn. Height of plant (as a concomitant of its vigor), length of ear, and

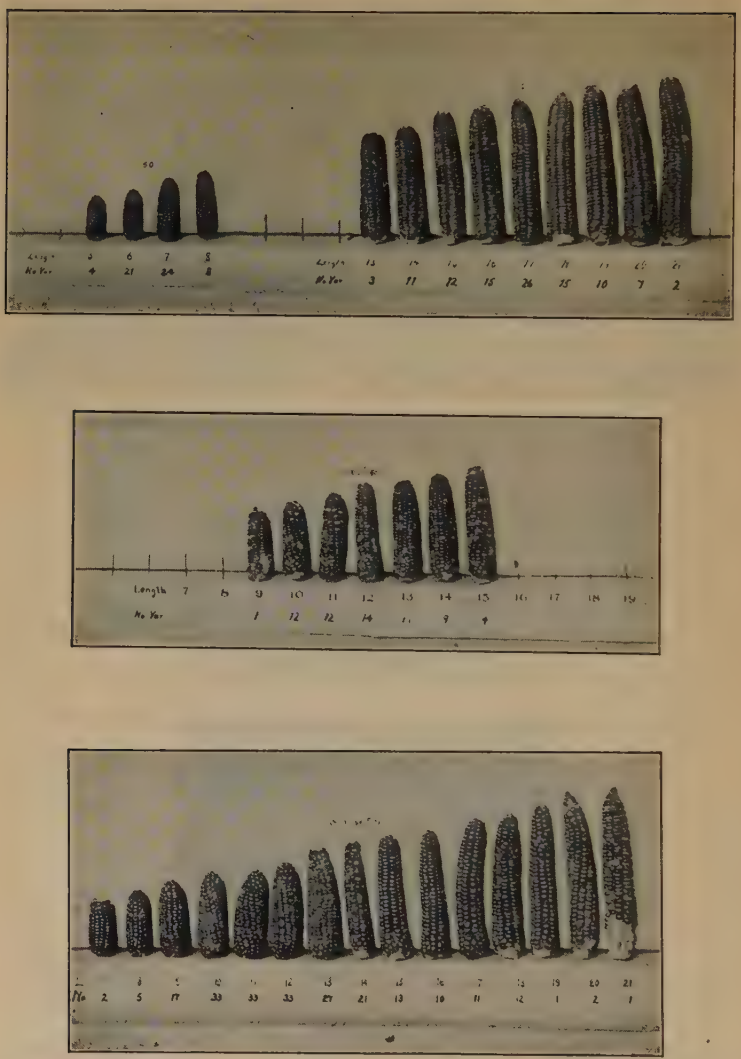


FIG. 59.—Top line; at left, Tom Thumb pop corn; at right, black Mexican sweet corn. Middle row; F_1 from crossing the above races. Lower line F_2 of same cross. (After East.)

productivity depend on multiple factors. For example, East crossed the strain Tom Thumb (having short ears) to black Mexican sweet (having long ears). The relative length of ear in these two races is shown in the upper line of Fig. 59, to the left and to the right. A sample of the F_1 ears is shown in Fig. 59, the middle of the figure, while the variability of the F_2 ears is shown in the lowest line. It is evident not only that the original types reappear, but that there are all intermediate lengths of ear in F_2.

These are only a few typical illustrations, selected from among many similar cases in which a small variability in F_1 and a larger, continuous variability in F_2 have been described. It should, however, be noted that these criteria taken by themselves do not constitute decisive proof of the existence of multiple factors in any particular cross. For even if only a single factor-difference is present, the disturbing action of fluctuation in the somatic manifestation of the factors may produce effects superficially very similar to those described above, provided the fluctuation is great enough to make the different types overlap in appearance. This is true especially in cases in which the dominance is incomplete. A good example of this kind is Morgan and Bridges' cross of flies with and without a trident pattern on the thorax (see Fig. 59*A*, I to X).
When the flies of the two parent races were classified according to the different grades of intensity of the marking (Fig. 59*A*), 1,614 of the lighter, or

"without," race gave curve a in Fig. 59*B*, and 2,538 of the "with" race gave curve b; it will be seen that these curves overlap. The 2,587 F_1 gave curve c, which shows the effect of incomplete dominance, together with a degree of dispersion about equal to that of the parental "with" race. The 3,100 F_2 gave curve d, which at first sight might be taken to indicate factor variability or the effects of recombination of numerous factors.

Fig. 59A.—Grades I to X, showing "without" to "with" patterns on thorax of Drosophila.

Curve e, however, shows the resultant which would be obtained by a combination of curves a, c, and b in a 1 : 2 : 1 proportion; the close similarity of this to the observed F_2 curve shows that the latter really represents a monohybrid Mendelian result. Had more factors been concerned, the deviation of the observed curve from the calculated would have been of a different type from that which occurred—fewer flies resembling the grandparents would have appeared rather than more, at least in the case of

one of the two grandparental types. As to the exact way in which the curve of the F_2 individuals in a case of multiple factors will differ from that in a monohybrid cross like the above, no definite rule can be formulated; the result will vary according to the number and mode of interaction of the multiple factors, but in any event the presence of the multiple factors may be detected by comparing

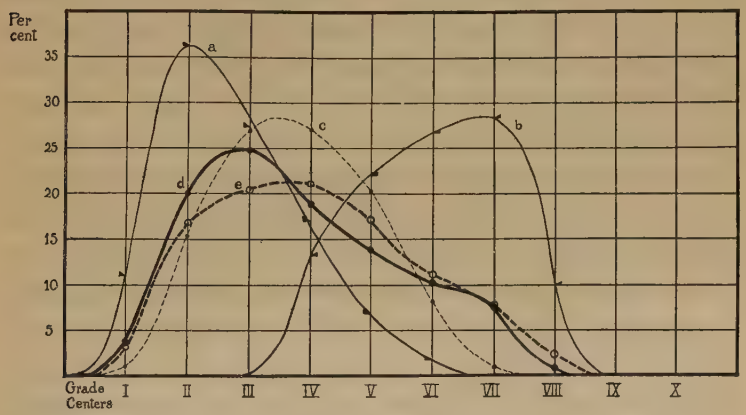


Fig. 59B.—Curves representing the distribution of grades of the trident pattern "with" in various stocks and crosses.

the observed curve with the one calculated from the parental and F_1 curves by the method used in the above experiment. The two curves should never be the same, and the multiple factor curve will almost always show a smoother, more even distribution, with less tendency to form a mode at each grandparental value.

In distinction to cases of single factor-differences, it should also be noted that in cases of multiple

factors the P_1 grades do not necessarily stand as the extreme limits of the values obtained in F_1 and F_2. It will often happen that the F_1, and, more especially, some of the F_2 combinations, will contain more factors (or rather, a more effective combination of factors) for a given character than either of the P_1 individuals possessed; for, each of the P_1 forms may have contained certain factors for the given character, but different factors in the two cases. This was true in the cross of black with ebony flies reported on page 228. It should commonly be the result where each parental race has separately been subjected to a process of selection in the same direction for the character under consideration, for in each line, factors favoring this character, will be conserved, as they appear, but in the two separate lines different sets of factors for producing such a result will tend to accumulate. In the case of "vigor," just such selective processes usually occur in nature, and as a result either parental limit is often transgressed in F_1 or F_2. On the other hand, where the two races have been selected in opposite directions, or where only one of them has been subjected to selection—as in the case of the fan-tail pigeons, lop-eared rabbits, and other fancy breeds—practically all of the differential factors tending to produce the given character are commonly present in only one of the parental races, and so only the extremes of the F_2 forms will reach either of the parental grades. In either type of case, however, the two characteristic signs of mul-

tiple cumulative factors are conspicuously present—namely, the great variability of the F_2 (or the back-cross), as compared with either of the P_1 or the F_1 groups, and the greater smoothness of its curve, as compared with that which would result by combining the P_1 and F_1 curves in 1 : 2 : 1 (or 1 : 1) ratio.

In certain cases showing characteristics of multiple factor inheritance, the interpretation has not at first been so clear as in the cases given above, owing to the existence of certain peculiar features which seemed rather to call for the assumption of genetic phenomena of totally different and hitherto undemonstrated sort, such as a continual fluctuation within the factor itself.

A case in point is that of truncate wing in Drosophila (Fig. 18, *b*), investigated by E. Altenburg and H. J. Muller, which was the first of these refractory cases to be solved. The race of truncate flies is never uniform: it usually throws flies with wings of various grades ranging all the way from short truncate to normal. It was attempted, through over 100 generations of selection, to obtain a pure stock, but although the proportion of truncates was raised to about 90 per cent., the normals were never eliminated completely, and the grade of truncation was still subject to much fluctuation. Crosses of truncates to wild type flies produce varying results: in F_1 0 to 8 per cent. show some truncation; in F_2 the proportion with any trace of truncation is highly inconstant, being sometimes as

low as 0 and rarely higher than 20 per cent.; in later generations, however, the proportion and the intensity of the extracted truncates may again be raised, by selection, to about 90 per cent. That the variation in truncation within the original highly selected stock, as well as within the extracted stock, is not merely a somatic effect due to uncontrollable environmental influences was shown by the fact that the variations in both lines were to a large extent heritable: selection of normals resulted in a much lower percentage of truncate offspring than were thrown by their truncate brothers and sisters, and selection of intermediates gave, on the average, intermediate results. The fact that such genetic differences are still constantly occurring in the original stock, in spite of the long-continued selection, seemed to indicate that here at least there was a case of instability of factors or contamination of allelomorphs.

An analysis of the factorial composition of the truncate flies was then made by crossing them to flies containing in each of their chromosomes other mutant factors whose hereditary behavior was known. In the second generation of the cross (back-cross) these other factors served as identifying marks which disclosed just which chromosomes of the P_1 truncate fly each F_2 individual had or had not received. By observing the amount of truncation which accompanied each ascertained combination of chromosomes it could thus be determined just what role each of the chromosomes played in

the production of the truncate character. By this means it was shown that in the production of this character there are involved at least three factors (T_1, T_2, T_3), one in the first, one in the second, and one or more in the third chromosome. The character cannot make its appearance without the factor in the second chromosome (T_2), but it may appear without either of the other factors, which are, therefore, in the nature of intensifiers. Moreover, truncate is influenced by still other factors. For instance, bar, a first chromosome factor, acts in much the same way as the ordinary first chromosome intensifier. The female factors intensify truncate, *i.e.*, truncate appears more readily in the females than in the males and may, therefore, be called partially "sex-limited." Especially noteworthy is the fact that while it rarely appears in F_1 when crossed to the normal gray it is generally dominant in an individual either homozygous or heterozygous for black.

This latter circumstance made it possible to study truncate as a dominant in heterozygous condition. As will appear later, this simplified the problem greatly, especially in determining whether or not (1) the factors for truncate are stable; (2) whether they are contaminated by their allelomorphs; (3) whether any factors are concerned other than those in the three groups mentioned.

In order to attack these questions recourse was had to the information that had been gained concerning the linkage of truncate with other factors

whose modes of transmission were known; the latter factors were again used as "identifying marks" in following the distribution of the factors for truncate. A truncate male containing factors for truncate in both its second and third chromosomes was mated to a normal winged female containing in its second chromosomes the factor for black, and in its third chromosomes the factor for pink. The male offspring of this mating will, therefore, have the formula $\frac{T_2 \text{ gray}}{\text{long black}} \quad \frac{T_2 \text{ red}}{\text{long pink.}}$ They will not contain T_1, as males derive all sex-linked factors from their mother. An F_1 male was then backcrossed to black pink females. Since there is no crossing over in the male, all the offspring of this backcross containing the "identifying characters" gray and red will be genetically identical, and like their father—unless the factors for truncate are unstable, or contaminated by their normal allelomorphs. The gray reds were not all alike in appearance, however, some being truncate, though most were long. Males of these two classes were then tested by mating them individually, again to black pink females. From the result of these matings it was clearly shown that the longs and the truncates produced almost exactly the same proportion of truncate, proving that they had been alike genetically.

It will be observed that these test matings of heterozygous gray red males to black pink females were of exactly the same type as the cross of F_1; consequently gray red males having the same

combination of chromosomes as before will once more have been produced (among other offspring); such males may therefore be obtained and back-crossed generation after generation, to black pink females. In this way, although the flies are continually crossed and kept heterozygous, a "pure line" may be maintained in the sense that the same chromosome combination is continually transmitted without recombination. Two such heterozygous lines were thus propagated for twelve generations, and selected for truncate and for normal wing respectively. At the end of that time they were found still to be unchanged and like each other in respect to the amount of their truncation. This proved that there could not have been any contamination or miscibility of the truncate factors with their allelomorphs, or any instability of these factors; the genetic variability of the original truncate stock must therefore have been due entirely to the recombination of multiple factors, which was prevented in the present selection experiment. It also follows that all of these differential factors for truncate must be located in the chromosomes (in the three large chromosomes), since only the recombination of such factors had been prevented by the experimental technique.

It remained to be determined why, in the original truncate stock, recombination of factors could still be going on, since the prolonged selection should in any ordinary case have long since resulted in a homozygous condition. Special tests were there-

fore made in which the distribution of the various component factors of truncate received from the two parents could be separately followed among their offspring, by reason of the association of the homologous truncate factors in the different parents with different linked factors for other characters. It was found by this means that none of the offspring may ever receive the chief factor, T_2, from both parents, even though the latter both carry it; T_2, in other words, acts as a lethal when homozygous and so a pure stock cannot be obtained. T_3, it was found, may exist homozygously, but in that case causes a marked reduction of fertility. This would tend to keep the selected stock impure for T_3 as well as for T_2. Such a stock should throw a much larger percent of normals than was actually obtained in the selected race; the relative deficiency of normals in the latter was evidently due to the presence of another lethal factor in the chromosome containing the normal allelomorph of truncate (see case of beaded below).

The case of truncate is of interest not only because the results indicate that other non-conformable instances might be similarly explained, but also because the new methods—involving linked "identifying factors"—which have been developed in attacking it are singularly adapted to the solution of such problems. The use of these methods has been made possible by the information at hand as to the arrangement of the factors in groups and as to the frequencies of crossing over. Without such

knowledge the case would have been practically insoluble.

Similar methods of attack have also been used by Dexter, and by Muller, in their experiments with the "beaded" wing of Drosophila (Fig. 60).

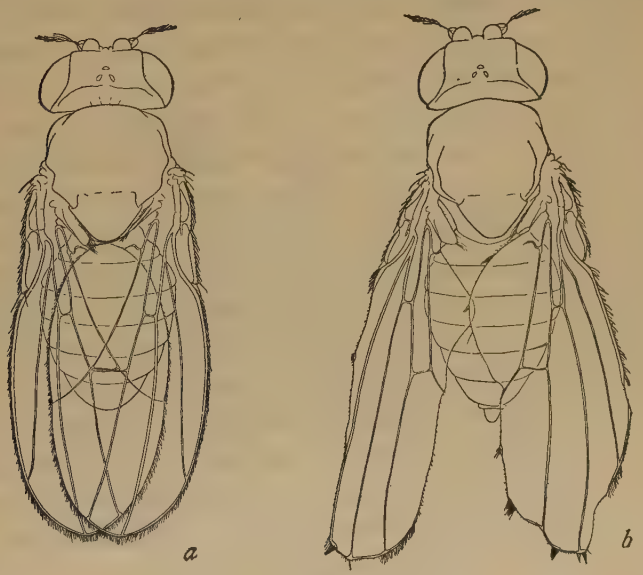


FIG. 60.—Normal wing (to left) and beaded wing (to right) of Drosophila.

The beaded character likewise is a variable one, some of the beaded individuals being very nearly normal in appearance. The degree of abnormality and the proportion of abnormal offspring are both capable of being altered, within limits, by selection or by crossing to normal stock.

Dexter crossed beaded flies to flies carrying

mutant factors in the different chromosomes and studied the linkage of the beaded character with these other characters. He found that beadedness showed linkage to third-chromosome characters, indicating that there is at least one factor for the character located in that chromosome. He also found that sometimes beadedness showed linkage to second-chromosome characters, while at other times it failed to do so. This indicated that the beaded stock was impure for a factor located in the second chromosome, which when present increases the amount of beading. Selection would be effective either by eliminating or by preserving this factor.

Later, Muller found, by means of linkage experiments, that the chief factor for beaded, lying in the third chromosome, is lethal when homozygous, but that the highly selected heterozygous stock also carries another lethal, lying in the homologous third chromosome in almost complete linkage with the normal allelomorph of beaded. Neither beaded nor its normal allelomorph, therefore, can exist in homozygous condition, and the stock breeds true to its heterozygous type. Since this "balanced lethal" stock had at the same time become homozygous for the intensifier in the second chromosome, it resulted that, although heterozygous for the chief factor, it had become "pure" for the character beaded. Further results with this stock will be considered in the last chapter.

An extensive selection experiment was carried out by Sturtevant on the character "dichaete,"

of Drosophila, which involves a reduction in the number of dorso-central and scutellar bristles. Pure dichaete stock cannot be maintained, since dichaete, like the chief factors in both the preceding cases, is lethal when homozygous, but the heterozygous dichaetes show the wing and bristle characters. Several different lines were maintained, some being selected in a plus direction, for a larger number of bristles, others in a minus direction. Quantitative studies were made of the bristle number of the dichaetes in each generation, and mean, standard deviation, and parent-offspring correlation were determined. Selection was apparently effective in changing the lines, and reversed selection seemed effective in certain instances. Whatever the source of the result may have been, there could be no doubt that the two sets of lines—plus and minus—showed significant differences from each other after the more than eleven generations of selection. Crosses made between these lines and races with known mutant factors in the second and third chromosomes proved that at least one pair of modifying factors for bristle number in each of these chromosomes was involved in causing the difference between the plus and the minus lines. The plus modifier in each chromosome was dominant to its minus allelomorph, when in a fly having the chief factor for dichaete. In flies without dichaete the modifiers had much less, if any, effect.

When a plus dichaete race was crossed to a minus, the F_1 resembled the plus parent more nearly,

and there was little increased variability, but in F_2 the variability was increased greatly: the extreme grades of the selected stocks again appeared, together with all intermediate values. The F_2 curve was not, however, one that could be reconstructed by simply compounding the P_1 and F_1 curves in 1 : 2 : 1 ratio as in Morgan and Bridges' cross of thorax pattern, for the proportion of intermediates was much greater than in a distribution so calcu-

FIG. 61.—Series of arbitrary grades of hooded rats used in classifying results of selection experiment. Above the figures the numbers assigned to the grades are given (see text). (After Castle and Phillips.)

lated; this again showed that more than one pair of modifying factors was involved.

One of the most exhaustively studied cases of the effect of selection on a mixed population is that carried out on hooded rats by Castle and his coworkers, particularly Phillips. The pattern of hooded rats is shown in Fig. 61. The dark pigment covers the head and extends as a stripe down the back. The extent of the hood and the breadth of the dorsal band are so variable that in one direction,

called plus, the rat is all black, except for a white stripe on the belly, and in the other direction, minus, the only black present is on the head.

Two selections were carried out: one in the plus direction (toward the darker type), the other in the minus direction (toward the lighter type). In the case of both lines steady progress in the direction of selection took place during the thirteen generations of the main experiment.

This progress in the direction of selection would be expected if the race were not at the start pure for factors that determine the amount of pigmentation, since in all such cases the process of selection in a heterogeneous population sorts out some of the factors from others. Selection in most cases creates nothing that is not already present, but separates existing factors.

There are several ways in which the composition of the rats after their selection can be tested, and some of these tests Castle and Phillips have made. When *light-colored* rats from the *minus* series were bred to wild or to Irish rats that had a uniformly (or nearly uniformly) dark coat, all the offspring had practically completely colored coats. When these were inbred they gave 3 uniform to 1 hooded coat. This result shows that there is one chief factor (which is recessive) for hooded coat. However, the F_2 hooded rats differed more among themselves than did those from the grandparental strain of hooded rats, which shows that other factors were involved as well, that modified the

extent of pigmentation of the hooded coat, but had little effect on the uniform coat. The range of variation was extended in the direction of the darker coat, showing that modifying factors causing a darker coat had been introduced from the wild strain; and such would be the expectation if selection had eliminated from the domesticated strain some of the factors making for the darker coat that had been present in the original impure population. Conversely the *darker* hooded rats, *plus* series, were bred to wild gray rats: the F_1 were uniform; these inbred gave 3 uniform to 1 hooded in F_2. The range of variation of the latter was again greater than that present in the dark hooded rats which had not been outcrossed, but now the range extended rather in the minus direction, *i.e.*, the F_2 hooded rats were on the whole lighter than their dark hooded grandparents. The result is what the multiple factor hypothesis calls for, if the wild or Irish rats contain factors that influence the condition of the color pattern. Plus selection had weeded out some of the "minus" factors, but crossing with a race in which no selection had been practised brought them back. When the selected plus and minus races were crossed to each other the variability was somewhat increased in F_1, and was further increased in F_2. The extreme conditions of the grandparents rarely appear in this generation. Again the results are those the theory calls for.

The test of reversing the direction of selection

was tried. The P_1 of the reversed minus line belonged to the 7 (and "$7\frac{1}{2}$") generation of the minus selection series. This generation had shown an average grade of -1.56, which represented a regression of 0.30 from those extreme individuals (-1.86) of generation 6 from which they had arisen. The range of generation 7 was from 0 to -2.50. Some of the low-grade offspring ranging from -0.37 to -0.87 were chosen for the return selection. They produced 118 offspring whose average was -1.28, a regression of 0.68, which is in the opposite direction from the regression obtained in the former (minus) selection. For six generations the reversed selection went on and carried the race back along its former course, *i.e.*, toward its original condition. The fact that selection in the original direction was still producing some effect when the reversed selection began, means, on the multiple factor hypothesis, that the stock was still heterogeneous, *in some factors at least*, and, therefore, reversing the process would be expected to give the results that Castle and Phillips obtained.

These important results of Castle and Phillips fulfil so entirely the expectation for multiple factors that they might have been utilized as a good illustration of the effects of selection on a group in which a particular character owed its modifications to multiple factors. The results are, however, of additional historical interest because they were used for several years as the favorite experimental "demonstration" for a very different conception. The

experiments had been begun to test the Darwinian problem of whether selection of a fluctuating character in a given direction would tend to further variation in the same direction, and so enable the establishment of a genetic type with a new mode, and a new range of variation. When Castle found that the selection was in fact successful in these respects, he interpreted the results to mean that through selection, or after selection, a "unit character" can be changed. He has used at times a word familiar to readers of Darwin, namely, "potency." The potency of a *factor* as well as of a character is supposed to be a somewhat variable element, and it was apparently presumed that this property of the factor was responsible for the observed fluctuation, rather than any recombination of modifying factors.

In support of the view that the particular character of the hooded rat differs from the wild rat by a single (fluctuating) factor, rather than by multiple factors, it was pointed out that the Mendelian ratio of 3 : 1 was obtained in the F_2 generation when these types were crossed. It should be observed, however, that this ratio only shows that a recessive factor for hoodedness must be present in order that the rats may be hooded at all. One-fourth of the rats will receive this factor and only these will appear as some grade of hooded. Other pairs of factors that modify the coat will be distributed independently of the former factor throughout the F_2 individuals, but they may produce

a visible effect only in the presence of this chief factor for hoodedness. The F_2 from the crosses to self-color indicate that such modifiers are really present in the rats, since the hooded F_2 are far more variable than their hooded ancestors. The understanding of this point is so important that similar relations of the same sort may be cited. If a chocolate mouse (*i.e.*, one that carries the factors for black and for cinnamon) is mated to a white mouse carrying the factors for gray (instead of those for black and cinnamon) the F_1 generation will be gray. In the F_2 there are three colored mice to one white one, but there are several sorts of colored mice. Color of any kind is dependent on the action of a factor allelomorphic to white, hence the 3 : 1 ratio, but this classification ignores the occurrence of several kinds of colored mice which are due to differences in other factors determining what kind of color will develop.

There are several cases in Drosophila that illustrate the same point. Eosin is a light eye color. Another factor called cream produces no effect on other eye colors, but makes eosin still lighter. A male pure for cream and for eosin bred to a red female gives red eye color in F_1. The F_1's inbred give three reds to one light eye color, but among the lights three different but overlapping kinds may be detected. Here, as in Castle's case, there is a *chief factor* (eosin) for reduced pigmentation, which must be present if any reduction in the color occurs at all, and another factor (cream) that

modifies the amount of pigmentation when the chief factor is present. Similarly the truncate and the beaded intensifiers produced an effect upon the wing only if their respective chief factor was present.

When it was recognized that the 3 : 1 ratio did not establish the view that only one pair of factors was being dealt with in the hooded rats, a new experiment was devised, by Wright, which was intended to discriminate between the effect of a single factor-difference, combined with fluctuating potency, and the effect of multiple factor-differences. It will be remembered that the plus race—which had an average grade at the time of +3.75—had been crossed to normal and then extracted in F_2, when it was found to have a somewhat lighter color— +3.17—than before. On the other hand the minus race— −2.54,—when crossed to normal and extracted, averaged in F_2 −0.38. If multiple factor differences were present, then if either extracted race were again crossed to normal and extracted it should be changed still more in the same direction, for it would come to contain an assortment of independent modifying factors more nearly like that in the normal race, even though it had the original factor for hoodedness. With each crossing and extraction the resulting hooded individuals should thus tend to approach more nearly to this same normal composition as a limit, and therefore they should also approach each other. On the other hand, if the differences between the hooded races lay in the potencies of their chief

factor, there was no known process whereby a result of this kind would be expected. Castle found, on performing the experiment, that when the minus hooded of first extraction (−0.38) were crossed to normal, the minus hooded of the second extraction averaged +1.01, and when these were again crossed, the minus of third extraction averaged +2.55, and did not range below +1.00. The plus race, after the second extraction, was apparently no further modified than before, being +3.34, there was even some change in the reverse direction; but this result seemed due principally to the peculiar factorial composition which one aberrant family happened to have received; after the third extraction further change was again noticeable, the average being +3.04. Moreover, some of the families were of almost exactly the same grade as some of those in the third extracted minus series. As a result of these experiments, Castle has reversed his earlier conclusion and states that the case is after all one of multiple modifying factors.

In favor of the view that factors are constant are the convincing experiments of Johannsen on the size of the Princess beans. The material is highly favorable for work of this kind, not only because exact measurements may be taken, but because the stocks reproduce by self-fertilization and were found to be homozygous. Johannsen's results (Fig. 62) show that no matter how many factors influence the size of the bean, so long as the bean is homozygous, selection of plus and minus variants produces no

effect on subsequent generations. Exactly the opposite results are expected when the population is heteroenegous for multiple factors at the beginning (see Fig. 62). In the latter case, selection of the mixed material will lead to the isolation of definite

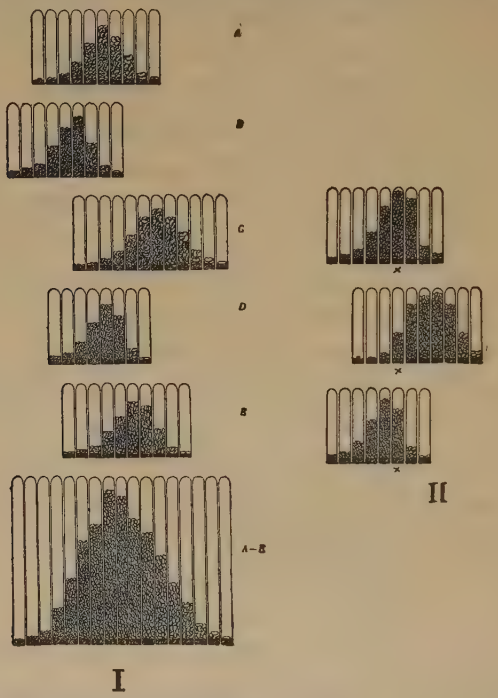


FIG. 62.—I. Five pure lines of beans (*A*, *B*, *C*, *D*, *E*), and the population (A–E) that results when they are mixed. II. The upper figure represents the original biotype, and the two figures below this, the two new biotypes that arose from it. (After Johannsen.)

types and even to the production of new types through recombination. This is the source of most of the success of the practical breeder.

To what has been said, however, one additional consideration must be urged. Mutations may occur

at any time and will be quickly observed if they are in the direction in which a selective process is being carried out. It may not be easy to recognize the first appearance of a mutant and, in fact, its presence may be detected only after the selection has gone so far that its origin is lost. The breeder may, if he is not extremely observant, infer that his selection is producing the desired effect on the potency of the character, while in reality he is studying the influence of a new factor on the character under selection. This possibility may be illustrated by two cases. In Castle's experiments two rats appeared that behaved like a new type. In fact he gives them the value of mutants. In Drosophila, Morgan carried out a selection experiment for three years, involving upward of 75 generations. The character selected was a dark "trident" on the thorax (Fig. 63). In a few generations a minus stock with no trident was established that bred true. The plus stock went up and down, the selection being not always thorough. A stock that always had the trident present to some degree was obtained after a time. Later several other mutations appeared, some of which greatly increased the black on the thorax; some even swamped the trident, making it a broad band. Three such mutant stocks were readily isolated. It might have been concluded that these mutations had occurred in the direction of selection, because selection had changed the potency of the trident factor, were it not that during these three years over 100 other

mutant characters had appeared in Drosophila, affecting every part of the body. Obviously when such changes are taking place everywhere, one would almost certainly find changes occurring in

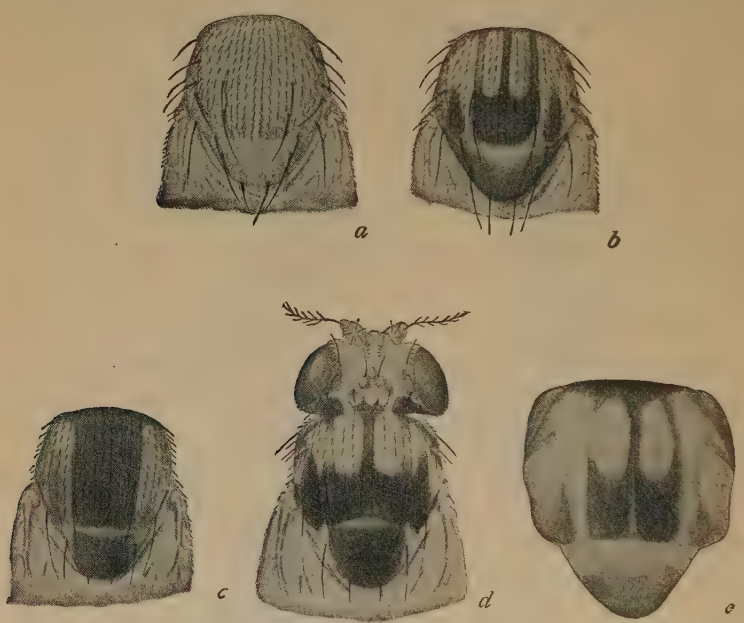


FIG. 63.—Thorax of mutant stocks of Drosophila ampelophila. *a*, race "without" trident; *b*, race "with" trident; *c*, race called streak; *d*, race called trefoil; *e*, race called band.

the parts that were being carefully scrutinized for any changes whatever.

Zeleny, in the course of a long series of selections for narrower and wider bar eye, found such mutations in both the plus and the minus direction. He determined that they took place in the chief factor for bar eye itself, thus establishing a series of

allelomorphs; the new types, like the old, were however highly stable genetically, and not to be confounded in any sense with "fluctuating factors." In addition to variation due to these mutations in the chief factor, differences in modifying factors have also been established between bar-eyed lines, in the experiments of Matoon and Zeleny, of Zeleny, and of May. In certain of these cases the stocks were evidently heterozygous for the modifiers from the beginning, but in other cases mutation seems to have occurred during the course of the experiment.

CHAPTER X

THE FACTORIAL HYPOTHESIS

In Mendelian heredity the word "factor" is used for something which segregates in the germ cells, and which is somehow connected with particular effects on the organism that contains it. For example, if a fly (♀) with red eyes is crossed to a fly (♂) with white eyes, there will be in F_2 three reds to one white, and this ratio can be explained by the assumption that in the F_1 hybrid something for red eyes has separated from something for white eyes.

We may express these factorial relations in another way by saying that a germ cell that produces white eyes differs from a germ cell that produces red eyes by one factor-difference. We think of this difference as having arisen through a factor in the red-eyed wild fly mutating to a factor for white.

Mendelian heredity has taught us that the germ cells must contain many factors that affect the same character. Red eye color in Drosophila, for example, must be due to a large number of factors, for as many as 25 mutations for eye color at different loci have already come to light. Each produced a specific effect on eye color; it is more than probable that in the wild fly all or many of the normal allelomorphs at these loci have something to do with red eye color.

One can therefore easily imagine that when one of these 25 factors changes, a different end result is produced, such as pink eyes, or vermilion eyes, or white eyes or eosin eyes. Each such color may be the product of 25 factors (probably of many more) and each set of 25 or more differs from the normal in a different factor. It is this one different factor that we regard as the "unit factor" for this particular effect, but obviously it is only one of the 25 unit factors that are producing the effect. However since it is only this one factor and not all 25 which causes the difference between this particular eye color and the normal, we get simple Mendelian segregation in respect to this difference. In this sense we may say that a particular factor (p) is the cause of pink, for we use cause here in the sense in which science always uses this expression, namely, to mean that a particular system differs from another system only in one special factor.

The converse relation is also true, namely, that a single factor may affect more than one character. For example, the factor for rudimentary wings in Drosophila affects not only the wings, but the legs, the number of eggs laid, the viability, etc. Indeed, in his definition of mutation, DeVries supposed that a change in a unit factor involves all parts of the body. The germ cells may be thought of as a mixture of many chemical substances, some of them more closely related to the production of a special character, color, for example, than are others. If any one of the substances undergoes a change, however slight, the end

product of the activity of the germ cell may be different. All sorts of characters might be affected by the change, but certain parts might be more conspicuously changed than are others. It is these more obvious effects that we seize upon and call unit characters. It is the custom of most writers to speak of the most affected part as a "unit character," and to disregard minor or less obvious changes in other parts. They frequently speak of a unit character as the result of a unit factor, forgetting that the unit character may be only one effect of the factor.

Failure to realize the importance of these two points, namely, that a single factor may have several effects, and that a single character may depend on many factors, has led to much confusion between factors and characters, and at times to the abuse of the term "unit character." It can not, therefore, be too strongly insisted upon that the real unit in heredity is the factor, while the character is the product of a number of genetic factors and of environmental conditions. The character behaves as a unit only when the contrasted individuals differ in regard to a single genetic factor, and only in this case may it be called a unit character. As soon as the individuals differ by two or more genetic factors that affect the same character the latter can be no longer considered a unit. So much misunderstanding has arisen among geneticists themselves through the careless use of the term "unit character" that the term deserves the disrepute into which it is falling.

In the following sections, several of the more important misconceptions arising from the confusion between factors and characters will be considered in turn:

1. There is a curious objection to the factorial hypothesis that is sometimes brought forward. It originated apparently as an objection to Weismann's idea that a single determinant stands for a single character. Weismann's idea of a sorting out of determinants undoubtedly implies something of this kind. The objection states that the organism is a whole—that the whole determines the nature of the parts. Such a statement, in so far as it has any meaning at all, rests on a confusion of ideas. That the different regions of the developing embryo do sometimes have an immediate influence on each other has been abundantly demonstrated, as well as the fact that in other cases parts have little or no influence on each other. That substances are produced in one place whose principal effects are seen in other places is not likely to be denied. It has even been insisted in the preceding pages that the evidence from heredity indicates with great probability that there are many factors whose combined effect is necessary for the production of each separate character, as in the production of eye color, for example. There is no reason why this interaction should always take place within the separate cells; in other words, why the products of factor A in one cell should not sometimes affect the products of factor B in another cell. The factorial hypothesis

does not assume that any one factor produces a particular character directly and by itself, but only that a character in one organism may differ from a character in another because the sets of factors in the two organisms have one difference. This point is not likely to be misunderstood by any one who grasps the meaning of the factorial hypothesis. The "organism-as-a-whole" argument, so long as it is not a vague and mystical sentiment incapable of clear expression, has no terrors for the factorial hypothesis, for this hypothesis disclaims any intention of making one unit character the sole product of one factor of the germ.

2. No one disputes that characters vary, but it has become necessary to explain what we mean by this statement. Many populations have been shown to be mixtures of different genetic types. This means that many of the individuals have different germ plasms. In man, for instance, there are blue-eyed, brown-eyed, black-eyed and pink-eyed individuals, and these variations of eye color have been shown by Hurst, the Davenports, Holmes and others to depend on different factorial constitutions. It has been shown in several cases, notably in corn, by Shull, and by East and Hayes, that populations may contain differences in many factors that have similar effects on the same character. In this case too the different factors that affect a part in the same way are shown to separate and recombine in successive generations. The result is variability, but variability of a sort that is compatible with the

invariability of the factors involved. When, however, these factors were sorted out so that strains became homozygous, some variability probably due to evironic differences still remained. That is, in addition to the variation due to recombination it has been found that even in pure races "unit characters" vary. Why, then, it may be asked, do not the factors that produce them vary also?

Johannsen's work on material of a kind suitable to give a definite answer to this question and by methods that have not been questioned, has brought out clearly certain facts only vaguely stated before. In a population of beans he found that each bean gave rise by self-fertilization to what he called a pure line. Each of the original beans proved to be homozygous for all of the factors involved. This was probably due to self-fertilization through many generations, a process that automatically produces homozygous lines. The weights of the descendants of any given bean gave a curve of frequency which was different from that of the whole population (Fig. 62). Within the group derived from one bean, however, it was found that any bean, whether heavier or lighter than the others, gave a curve exactly like the curve of the line from which it came. Evidently then the size differences within these pure lines are not inherited. They must be due to the environment of the plant, or to the position of the bean in the pod, etc.; in other words to conditions that are extrinsic to the germ plasm. Here is a demonstration that the factors do not vary, but give identical results in successive

generations. Of course this demonstration could not have been made with heterozygous individuals.

3. It has also been suggested that one factor may sometimes contaminate its allelomorph, when the two meet in the hybrid. There is no *a priori* reason why this might not occur so far as we can see. The question is whether there is any evidence to establish or even make probable such a view. The great body of Mendelian evidence points unmistakably to the conclusion that as a rule contamination does not occur. It will require equally clear evidence to show that contamination does sometimes take place. Until this evidence is forthcoming the facts which have been said to support the hypothesis of contamination find a more consistent explanation on the hypothesis of multiple factors.

4. Bateson has recently argued from the visible differences between characters that a process of fractionation of factors takes place. The argument is given in the following quotation:

"Some of my Mendelian colleagues have spoken of genetic factors as permanent and indestructible. Relative permanence in a sense they have, for they commonly come out unchanged after segregation. But I am satisfied that they may occasionally undergo a quantitative disintegration, with the consequence that varieties are produced intermediate between the integral varieties from which they were derived. These disintegrated conditions I have spoken of as subtraction—or reduction—stages. For example, the Picotee sweet pea, with its purple edges, can surely

be nothing but a condition produced by the factor which ordinarily makes the fully purple flower, quantitatively diminished. The pied animal, such as the Dutch rabbit, must similarly be regarded as the result of partial defect of the chromogen from which the pigment is formed, or conceivably of the factor which effects its oxidation. On such lines I think we may with great confidence interpret all those intergrading forms which breed true and are not produced by factorial interference.

"It is to be inferred that these fractional degradations are the consequences of irregularities in segregation. We constantly see irregularities in the ordinary meristic processes, and in the distribution of somatic differentiation. We are familiar with half segments, with imperfect twinning, with leaves partially petaloid, with petals partially sepaloid. All these are evidences of departures from the normal regularity in the rhythms of repetition, or in those waves of differentiation by which the qualities are sorted out among the parts of the body. Similarly, when in segregation the qualities are sorted out among the germ cells in certain critical cell divisions we can not expect these differentiating divisions to be exempt from the imperfections and irregularities which are found in all the grosser divisions that we can observe."

Bateson has assumed because the character appears to fractionate that we are to infer that some particular factor, that stands for it, fractionates too, but such a conclusion overlooks the fact that a character is produced by many factors in co-operation,

and that, in consequence, many factor differences may occur which will, in turn, cause the character differences in question. Secondly, Bateson argues that we should expect these irregularities to occur in the segregation of character-factors during germ-cell formation, because we find irregularities in the segregation of factors during development. Apparently Bateson holds the view that differentiation of characters is the result of sorting out of factors in the somatic divisions; in other words, he adopts Weismann's theory of embryonic development. Localization of factors is inferred from localization of characters. Hence his employment of the idea chiefly when patterns are involved. The conclusion to which most modern students of experimental embryology have arrived, a conclusion based on a considerable body of evidence, is that differentiation is not a consequence of sorting out of the hereditary (genetic) materials. This conclusion is not considered or else is ignored by Bateson in this argument.

5. The confusion of character with factor is nowhere more apparent than in the well-known presence and absence hypothesis, and since this hypothesis has been so widely employed in Mendelian literature it calls for somewhat more extended analysis. The hypothesis was first proposed to explain the inheritance of combs in poultry (Fig. 64). Rose comb by single comb gives in F_2 three rose to one single; pea comb to single gives in F_2 three pea to one single. When rose is bred to pea a new type of comb, called walnut, appears, and in F_2 there are nine walnut:

three rose: three pea: one single. Since single comb was not present in either of the grandparental strains,

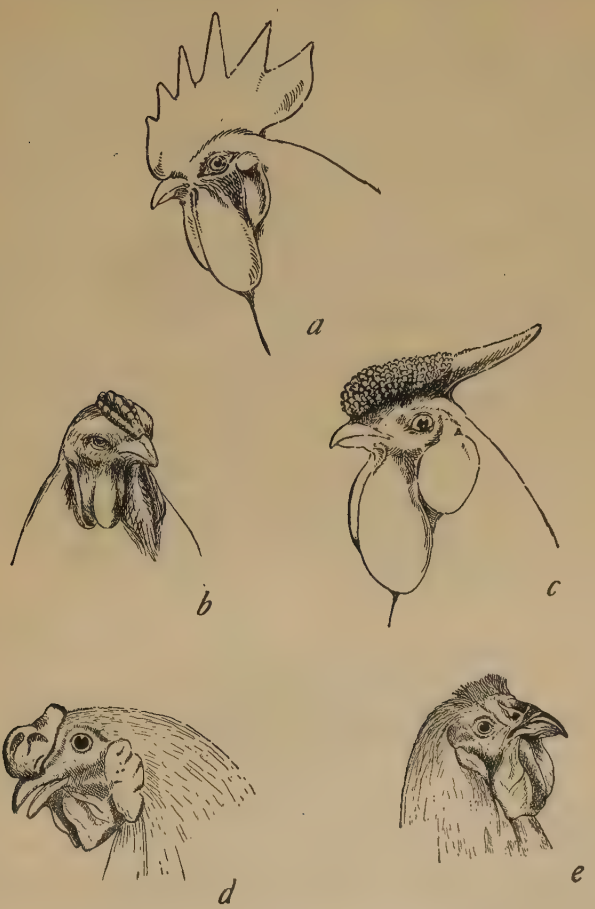


FIG. 64.—Combs of fowls. *a*, Single; *b*, pea; *c*, rose; *d*, walnut; *e*, Breda.

how then can its appearance in this cross be explained? The difficulty was met as follows: The ratio shows

clearly that two pairs of Mendelian factors are present. Pea comb was assumed to lack a factor for rose, and rose was assumed to lack a factor for pea. By recombination there should result in F_2 one individual in sixteen that was no-rose no-pea. This is the single comb. A single letter or symbol S was inserted in all of the formulæ so that when neither rose nor pea comb was present something would seem to be left to represent the single comb.

The verification of the latter point was supposed to be found in the relation of the single comb to a combless condition found in the Breda race of fowls, which, when crossed to single, gave in F_2 three singles to one combless. In other words the combless fowl was supposed to represent a race in which the lowest stage of the series had been reached and the last factor for comb had been lost. The series just described was represented on the presence and absence scheme as follows:

Rose	RpS
Pea	rPS
Walnut	RPS
Single	rpS

There is, obviously, no necessity to make these characters depend for their expression on *losses* of something; for the small letters that here stand for absences might just as well stand for actual factors different from those represented by the large letters. The formulæ would then of course work out as well as before. To those accustomed to the presence and

absence scheme it may, however, be difficult to think of the small letters as anything but absences. It may, therefore, be helpful to represent the same formulæ with other letters.

If the original comb was single, which in fact is the type of comb of the wild bird from which the domesticated races have come, a dominant mutation from A to A′ gave rise to a rose comb; another dominant mutation from the wild type that changed B to B′ gave rise to a pea comb; a third but recessive mutation that changed C to C′ gave rise to a "combless" comb. The normal allelomorphs would be represented by the same letters without the primes. The formulæ (in simplex) for the combs would then be as follows:

Wild type (single)	A B C
Rose	A′B C
Pea	A B′C
Combless	A B C′

The walnut comb that appears when pea is bred to rose is, of course, the double dominant form A′B′C.

If it seems desirable to use letters that give a clue to the name of the factor for which they stand, either of the next alternatives would cover the case under discussion. In the second of these the small letters are not absences, but only the recessive allelomorphs.

Wild type (single)	P R C or p′r′C
Rose	P R′C or p′R′C
Pea	P′R C or P′r′C
Combless	P R C′ or p′r′c

It is a matter of little theoretical importance what system of symbols is adopted, unless that system proves to be impracticable, or unless it implies relations that are unnecessary or unjustifiable. (See Appendix.)

We do not wish to appear to base our objection to the presence and absence hypothesis on the impracticability of its nomenclature in a new field, but rather on the grounds that the conception of presence and absence assumes that we do know something about the relation between character and factor that we can not possibly know. To assume the absence of a factor from the absence of a character is, in a sense, as naive as it was to assume that an animal moved toward light because it liked the light.

It need not be denied that losses of factors may occur, and it may even be probable that a loss in the germ plasm might lead to a loss in some part or parts of the body, but there still remains no justification for the assumption in any given case that we can infer from the lack of a character in an animal or plant a loss of factors. Such an assumption is entirely gratuitous; and gives a totally false impression concerning the factorial hypothesis of Mendelian heredity. Moreover, if taken literally it may lead to unwarranted conclusions in other fields.

It is similarly naive to assume the absence of a factor from the recessiveness of the character, yet the literature abounds with instances where the recessiveness of the character is taken as a criterion for

assuming the absence of the factor, the dominant character being considered as a "presence." Dominance, however, is often found to be incomplete if exact quantitative studies are made. In fact, characters are known to show all degrees of dominance and recessiveness over their alternative allelomorphs. Which character is to be considered dominant and which recessive when each allelomorph has an equal effect, as in the case of the red and the white Mirabilis, is entirely a matter of choice. Hence, no matter whether red or white is presence, the present factor is not truly dominant. It seems reasonable, then, to suppose that if presence and absence is true a hybrid (with one presence) might approach more nearly the type with two absences than to the type with two presences. In such a case the present factor would actually be the recessive. Such a case is in fact known. In the cross of horned by hornless sheep, the horned condition dominates in one sex and the hornless in the other. Here no matter which is considered as a presence it must be conceded that in one sex or the other it is recessive. The view that dominance of a factor proves its presence and recessiveness its absence should therefore be abandoned.

A further argument against the theory of presence and absence is found in the evidence, already given, which indicates the possibility of multiple allelomorphs. On the presence and absence system, only two kinds of allelomorphs, the presence and the absence, are possible, and no character differences

can be due to different kinds of factors, all of them "presences."

A word here may not be out of place concerning inhibitors. As pointed out, the adherents of presence and absence generally interpret the absence of a character to mean the absence of a factor; they also interpret recessiveness to mean the absence of a factor. When cases come up in which a character is absent, as horns in cattle, but the absence of the character is dominant, an attempt is made to reconcile fact and theory by assuming that the factor for the absent character is not really absent, but that an inhibitor is present whose activity prevents the appearance of the character.

Those who do not accept the presence and absence hypothesis need make no such assumption here of course. To them there is no reason why a factor for hornless should not dominate a factor for horns. Moreover, the facts do not even require one to assume that the hornless race differs from the horned because of the lack or inhibition of certain reactions, for it is possible in such cases that the reaction merely takes a different course, or may even proceed beyond the usual point.

These statements are not, however, intended to mean that factors may not at times act as inhibitors, but rather that we do not know, and in most cases can not know, in a single case enough about the nature of the reaction to demonstrate the existence of a factorial inhibitor.

Weismann's Præformation Hypothesis and the Factorial Theory

Weismann's theory of *development* postulates particles in the germ plasm that are sorted out in proper sequence to appropriate parts of the body as the embryonic cells divide. What determines the order of the sorting out of the factors was not explained. Weismann's speculation differed from other præformation theories mainly in that he made use of the chromosomal mechanism not only to carry the hereditary materials, but also to bring about the sorting out of the materials in order to reach their final destination in the body. His theory as applied to embryonic development failed, both because the facts concerning the behavior of the chromosomes during segmentation of the egg gave no support to his assumption of sorting out of the materials of the chromosomes, and also because the data from experimental embryology and regeneration indicated very clearly that no such sorting process takes place. On the other hand, Weismann's ideas of *heredity* concerning the segregation in the reduction divisions of the egg and sperm of inherited materials present in the chromosomes, furnish the basis of our present attempt to explain heredity in terms of the cell.

In common with Weismann's theory, the factorial theory of heredity rests on the assumption that the germ plasm contains a host of elements, that are independent of each other in the sense that one allelomorph may be substituted for another one without

alteration of either, and that these allelomorphs will now perpetuate themselves unchanged although in company with different factors. Today this assumption is no longer an *a priori* deduction, but a conclusion from experimental data.

The second real and important point of agreement between the factorial theory and Weismann's theory is that both maintain that at one period in the history of the germ cells, factors of diverse origin separate from each other in an orderly manner, half of them going to each pole. The precise way in which this is supposed to take place differs greatly on the two views, but the essential point is the same. We owe to Weismann more than to any other biologist the conception of segregation at the reduction division of the egg and sperm—a conception of fundamental importance in the application of the chromosome theory to Mendelian heredity.

The factorial theory as such deals with the behavior of its factors in an abstract way, quite apart from any material basis of which they may happen to be composed. In this way it may measure their constancy, segregation, linkage, etc. But the biologist is not likely to stop here, for, to him the problem involves cells about whose history and processes he has come to know certain facts. Weismann, following Roux, was the first to point out that these facts give a mechanism showing how separation of factors might take place. The specific application of the behavior of the chromosomes to heredity, then, is the third important contribution which modern genetics owes

to Weismann. Today, however, we have advanced beyond Weismann in this respect, and may more specifically interpret our numerical results of independent segregation, linkage, and even crossing over on the basis of a chromosome mechanism. Moreover, the new facts have given us ideas very different from those of Weismann regarding the arrangement of the factors in the chromosomes and the way in which the characters of an individual are determined by the chromosomal factors.

In the last edition of his Vortræge ueber Descendenztheorie (3d edition, 1913) Weismann modifies his earlier views in regard to the factorial nature of the chromosomes so that his conception of the germ plasm is brought into harmony with the Mendelian theory of heredity. Formerly he had supposed that the chromosomes are all alike, or nearly alike, in so far as each one carries a full assortment of "ids." Each id, in itself, represented the full complement of all the factors that go to make up the organism. But since the results of Mendelian heredity show that all sorts of characters, however trivial, may be segregated independently (which would not be the case, if, as Weismann formerly supposed, all the hereditary characters are carried by each chromosome), it follows that the chromosomes must be bearers of part ids (Theil Ids).

Weismann still adheres nevertheless to his mosaic theory of development, but as before stated the modern work on development does not support this interpretation of development. His view assumes

disintegration of the germ plasm when the body cells are produced in order to account for the localization of characters; the other view, following the experimental results and microscopical observations, assumes, so far as the chromosomal materials are concerned, that all of the hereditary factors are present in every cell in the body. This view is essentially that proposed by DeVries in his book on Intracellular Pangenesis. The cause of the differentiation of the cells of the embryo is not explained on the factorial hypothesis of heredity. On the factorial hypothesis the factors are conceived as chemical materials in the egg, which, like all chemical bodies, have definite composition. The characters of the organism are far removed, in all likelihood, from these materials. Between the two lies the whole world of embryonic development in which many and varied reactions take place before the end result, the character, emerges. Obviously, however, if every cell in the body of one individual has one complex, and every cell in the body of another individual has another complex that differs from the former by one difference, we can treat the two systems as two complexes quite irrespective of what development does so long as development is orderly.

It is sometimes said that our theories of heredity must remain superficial until we know something of the reactions that transform the egg into the adult. There can be no question of the paramount importance of finding out what takes place during development. The efforts of all students of experimental

embryology have been directed for several years toward this goal. It may even be true that this information, when gained, may help us to a better understanding of the factorial theory—we can not tell; for a knowledge of the chemistry of all of the pigments in an animal or plant might still be very far removed from an understanding of the chemical constitution of the hereditary factors by whose activity the pigments are ultimately produced. However this may be, the far-reaching significance of Mendel's principles remains, and gives us a numerical basis for the study of heredity. Although Mendel's law does not explain the phenomena of development, and does not pretend to explain them, it stands as a scientific explanation of heredity, because it fulfils all the requirements of any causal explanation.

CHAPTER XI

HEREDITY IN THE PROTOZOA

While certain characteristics or processes in the Protozoa have been shown to be transmitted along fission lines, and in this sense to be "inherited," nevertheless it is a fact that almost nothing has been found to show that single characters are segregated in a Mendelian sense, although there are indications that segregation of some sort takes place after conjugation. It may therefore appear questionable to use the word heredity, except in a very general way, in describing what occurs in the Protozoa.

Nearly all of the cases studied in protozoa relate to fission lines, *i.e.*, to individuals that have been produced by continued division of parent individuals, each giving rise to two daughter individuals. In such asexual reproduction it has been commonly assumed, on the basis of observation, that both micronucleus and macronucleus are divided into identical parts, and that the cytoplasm likewise is divided into equivalent halves. In regard to the cytoplasm, the halves are at first generally unlike; in the more highly specialized forms of infusorians the ends of the body are differently organized, and these differences may persist through the division, but are at once set straight by regeneration of the

missing parts. Should one end happen to have some local peculiarity or abnormality, this may be "inherited" through that half, but not by the other half. The abnormality may be said to be persistent rather than to be inherited.

Fission of protozoa is generally compared with cell-division in the soma of higher forms. It is known that here the two daughter-cells receive the chromosome complex of the mother cell and usually like parts of the maternal cytoplasm. When, as often occurs in early embryonic cells (blastomeres), the two daughter-cells get very different proportions of the visible inclusions of the original parent cell (such as pigment, or yolk) it has been shown by centrifuging experiments that such inclusions do not have a differentiating influence on the cells that contain them. Embryonic differentiation might however be influenced by other materials laid down regionally in the egg and not displaced by centrifuging. So far as known, such materials would have no permanent effect upon inheritance unless they were of a plastid character and capable of independent multiplication. It is customary, therefore, to consider all daughter cells as inheriting the entire genetic complex of the mother cell, and differentiation is ascribed to other influences than to sorting out of hereditary materials. It is referred to the environment in the widest sense, including the relationship (physical and chemical) to neighboring cells, and to the external surroundings of the whole embryo.

Similarly in asexual reproduction through buds, stolons, tubers and cuttings, the new plants inherit the parental complex, and breed true as they would have done had they remained a part of the original

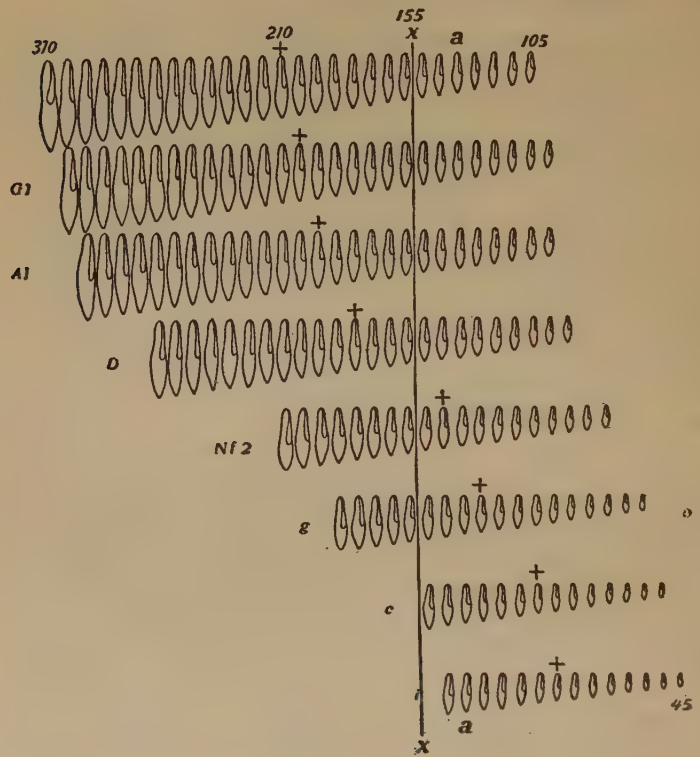


Fig. 65.—Diagram showing variation in 8 pure lines of Paramoecium. (After Jennings.)

plant. Here again if plastid inheritance appears, it is regarded as a special sort of inheritance that involves a mechanism different from that of Mendelian inheritance.

If these ideas are carried over to the Protozoa we might anticipate that daughter individuals would retain the characteristics of the parent cell from which they came, and in general this is true. Yet there are also records where selection of sister-individuals may form the starting point for separate lines that differ in definite ways. Our problem then is to determine, if possible, what mechanism is concerned in such results, how such differences arise, and in what sense they may be said to be inherited. The following evidence throws some light on these questions.

Jennings finds that in any mass culture, or in any pond, there are generally present several races of paramecium besides the two standard types of P. caudatum and P. aurelia. By breeding from single individuals he separated from a certain mixed culture at least eight lines differing mainly in size (Fig. 65). Later Jennings and Hargitt have separated still other races of paramecium. Within such races there is some fluctuating variability due to environment, age, etc.; but any one of the individuals, whether large or small, will give rise to a population that shows the same variability about a mean as was shown by the race from which the individual had been chosen.

Later Middleton (1915) working in Jennings' laboratory studied the same problems in a different infusorian, Stylonichia pustulata, that produces fission lines in the same way as does paramecium. Starting with a single individual he subjected the

descendants to selection, the basis of which was the rate of fission. For example, in one experiment he selected fast and slow lines starting with sister individuals. Repeating this selection for 130 days he found that the division rates were slowly increased or decreased. If the excess of generations produced by the fast-selected line is expressed "as a percentage of the total number of generations produced by both sets the difference is 6.9 per cent. for the first thirty days; 12.8 per cent. for the next twenty days; 19.3 per cent. for the next thirty days; and 21.2 per cent. for the last fifty days." The number of generations produced per line during 130 days ranges for the first lines from 178 to 187, and for the slow line 116 to 128. "The slowest fast-selected line produced 50 more generations than the fastest slow-selected lines." The difference that had arisen between the two lines was shown to be inherited in the following way. At intervals some of the individuals were reared without selection or else by "balanced selection." Thus after 80 days of selection two sets were subjected to no-selection. It was found that the culture for fast-selection lines still maintained the higher rate. In another test, a difference that had been produced by 80 days of selection, lasted for 102 days without selection. When reversed selection was carried out, however, the inherited difference was lost "in the same way that it was produced." Moreover it was found that if conjugation occurred in the fast set or in the slow set

"the difference produced by selection continued to exist after conjugation." It appears that some kind of change had been produced, and that the change in rate was inherited after selection ceased.

More recently still Jennings (1916) has carried out an elaborate experiment with another Protozoan, Difflugia corona (Fig. 66). This form also shows "in nature" great variability, due, it appears, to several or to many races often existing in the same locality. If any individual is taken as the starting point for a new population, it is found that the fission line that results is composed of individuals that are more like the parent than like members of the wild population taken as a whole. In other words each individual tends to transmit its peculiarities to its offspring, Fig. 67. Jennings then showed that selection within a pure line, *i.e.*, in a population descended from a single individual by fission, brings about a change in the direction of selection and that this change remains at least for a time after selection ceases.

The characters that were examined included the number of spines, the length of the spines, the diameter of the shell, the depth of the shell, the number of spines around the mouth, the diameter of the mouth. Through selection many diverse lines were produced in a strain coming from one original individual. The selection was based not only on individual differences, but also on "past performance."

Selection was often made by picking out extreme

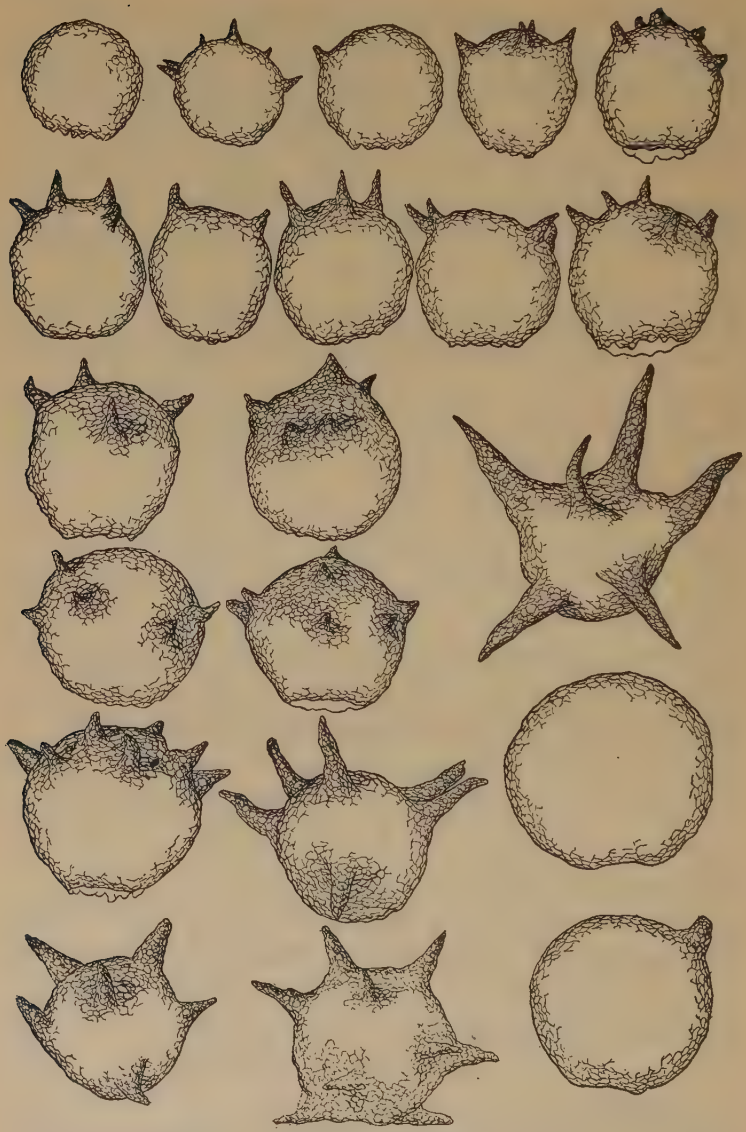


Fig. 66.—Collection of individuals of Difflugia corona, to show the variations in size and form, in number, length, and shape of the spines, etc. (After Jennings.)

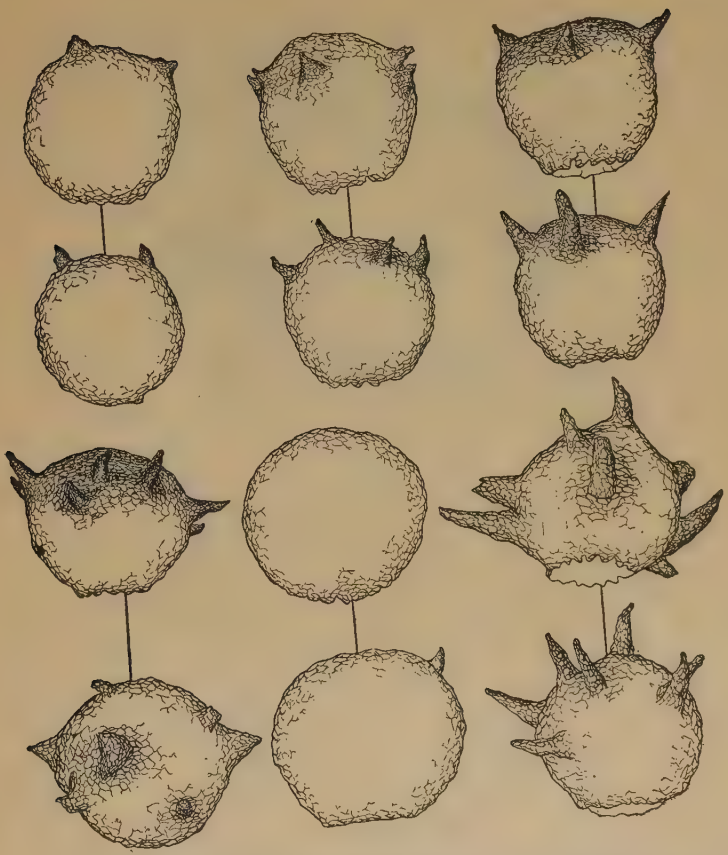


Fig. 67.—Parent and immediate offspring in 6 diverse strains or families of Difflugia corona, to show the variation and the inheritance by the progeny of the parental diversities. (After Jennings.)

individuals, and allowing their offspring to multiply, forming a population. The members of such a group were then measured. It was found that the character at first selected was present in the offspring. In some cases selection ceased after a certain peculi-

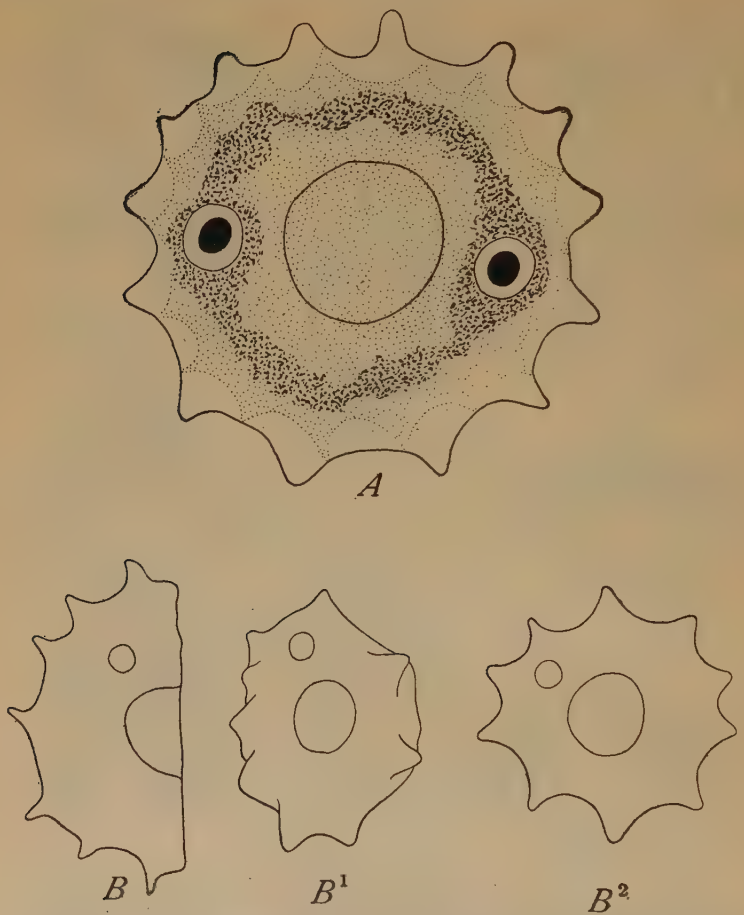


Fig. 68.—Arcella dentata. *A*, normal individual with two nuclei. *B*, individual cut so as to include only one nucleus. B^1, offspring of B B^2, offspring of B^1. (After Hegner.)

arity had been produced. The effects of the previous selection were still observable after several generations had passed, although the difference sometimes declined.

Hegner has studied similar problems on another form, Arcella dentata (Fig. 68), in Jennings' laboratory, and has fully confirmed Jennings' and Middleton's results. Hegner has made a number

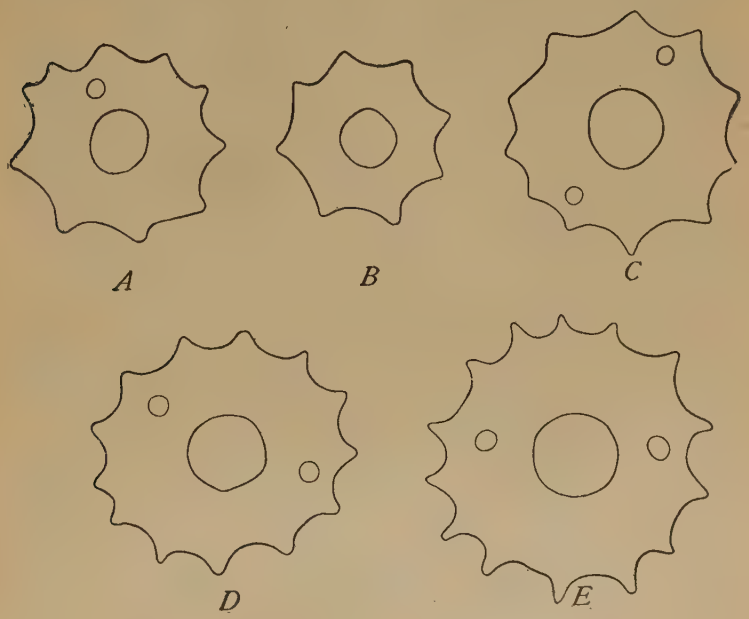


Fig. 69.—Arcella dentata. *A*, mononucleate individual. *B*, nonnucleate, and *C*, binucleate individual, products of division of mononucleate individual. *D*, descendant, and *E*, later descendant of *C*, approaching normal size. (After Hegner.)

of other experiments and observations that have a bearing on the influence of the nuclei and of the chromidial net of Arcella. In one species, A. dentata, there are two nuclei situated opposite to each other as seen in *A*, Fig. 68. If an individual is cut in

two pieces, the cut passing between the two nuclei, each half will remain alive and later continue to reproduce by fission. The first offspring produced are smaller than normal, and contain but a single nucleus (B^1 in Fig. 68). The offspring that they produce are in turn larger (B^2 in Fig. 68). They may still possess only one nucleus. But soon a division takes place of such a sort that an empty shell is formed (A–B in Fig. 69), while the mother individual that produced the empty shell is now found to contain two nuclei and has increased in size (C in Fig. 69). Its next offspring is still larger, and in the next or in a later generation the full size of the Arcella is regained.

There is present in Arcella a net of chromidia (A in Fig. 68), that forms a ring around the space between the two nuclei. A portion of the protoplasm was cut off by Hegner in such a way that some of the chromidial ring was removed although both nuclei remained. When the operated individual gave rise by fission to a daughter, the latter was smaller than normal. Hegner attributes its size to the smaller amount of cytoplasm in the mother at this time, and not directly to the loss of chromidia. When the daughter in turn produces a daughter, it is found to be normal or to more nearly approach the normal size. It is apparent, then, that if the initial decrease is ascribed to the loss of chromidial material rather than to protoplasm in general, it must be admitted that Arcella can sooner or later make good the loss sustained. It may seem doubt-

ful, therefore, whether one can safely appeal to unequal division of the chromidial mass as the means by which the selective process becomes effective. On the other hand, there is evidence from other observations that Hegner has made that may seem to furnish at least a clue to the agent through which the selective process takes place. Let us examine this evidence.

In one species, Arcella polypora, there is a variable number of nuclei ranging from 3 to 10. The diameter of the shells correspondingly ranges from 25 to 33 units. The number of these nuclei may change, and if large or small individuals are selected it is found that the larger individuals have more nuclei than the smaller ones. The change takes place before or during the selection period, but is not supposed to be directly affected by the selection itself. The larger individuals that are picked are larger because they have more nuclei, and the small ones are smaller because they have lost one or more nuclei. The change occurs at irregular intervals, and consists generally in an increase or decrease of one nucleus. "In several cases the number of nuclei doubled from 3 to 6." It was found also that the diameter of the shell and the number of spines are closely correlated, so that when selection was made for more spines, the size also increased, and *vice versa*. It is possible, therefore, that when selection of specimens took place, what was really selected was variations in the total nuclear mass. It is true that there were

certain families whose members possessed a larger number of nuclei but were smaller in diameter. It is evident, therefore, that other factors than nuclei *number* are also present. Possibly the amount of chromatin in the nuclei of these families may be different.

Since selection was also effective in Arcella dentata, which has consistently only two nuclei, the results here cannot be ascribed to an increase in the number of nuclei, but Jennings has suggested for Difflugia that "the substances determining the hereditary characters may be distributed with less accuracy than in the higher organisms, so that the two products of fission may often receive parts that are not equivalent." Hegner thinks that this may be true for Arcella and adds "The sudden large heritable change (mutations) would, according to this suggestion, be due to large qualitative inequalities, and the smaller heritable variations to smaller qualitative inequalities during nuclear division." Root (1918) has likewise carried out selection experiments with Centropyxis and has recorded changes following selection.

How these changes are brought about in the Protozoa is by no means evident. Jennings has not committed himself to any one interpretation. If we were to accept an old and now discredited view as to the influence of selection on any "fluctuating" character, it might appear that that view was confirmed, namely, that *any* change that appears in an individual will serve as a starting point for

further changes in the same direction under selection. If the first change noticed were due to a mutation, then the results would not be different in principle from those that are observed in higher forms, except that it would be necessary to assume that such mutational changes are far more frequent than is the case in those higher forms that have been investigated. There is also the possibility that in the Protozoa the division of the chromatin is not as precise as in the ordinary mitotic division of higher forms. In fact, when we turn our attention to the macronucleus we find that there is no convincing evidence to show that this nucleus divides with the same precision as do the chromosomes of the Metazoon cell. Lastly, there is the further possibility of unequal distribution of extranuclear chromatin (chromidia), which may in some cases furnish a basis for the differences observed in the selection experiments.

Recently Erdmann ('20) has shown in paramecium that progressive changes in form take place between two endomictic periods, hence some doubt is cast on the value of the earlier results that took no account of such a possibility. Moreover, Erdmann thinks that after endomixis many new lines may appear. If so, this throws further doubts on the value of the interpretation of the earlier experiments in which endomixis was overlooked. Still other doubts arise in consequence of Jollos' work ('21), described below.

Dallinger had experimented in 1887 on the effect

of raising the temperature of cultures containing certain flagellates. In the course of seven years he succeeded in producing a strain that could live at a temperature of 70° C., although at first the entire culture would be killed at a temperature of 61° C.

Recently, Jollos ('13–'14) caused Paramecium caudatum to acquire a resistance to compounds of arsenic. At first the individuals were killed when 1.1 parts of a standard solution were added to 100 parts of water. Gradually they became accustomed to live in 5 parts to 100. For several months they retained their acquired resistance when returned to their original environment, but they lost it at last. The loss was slow in fission lines, but sometimes sudden after a conjugation period. Jollos calls this sort of an induced change, "Dauer-modification," or long-persisting modification. He believes that it has nothing to do with a nuclear change in the hereditary constitution; *i.e.*, it is not a mutation at all but is probably a change in the plasma or in the macronucleus. The latter is absorbed during conjugation, also during parthenogenesis, hence the sudden disappearance of the Dauer-modification at this time. On the other hand, certain kinds of these modifications may even survive a conjugation period. For instance, after the changes induced by calcium treatment or by high temperature treatment the effects may survive for a long time if only fission takes place; they may survive several parthenogenetic periods, or even a conjugation

period, but ultimately there is a return to the original "reaction-norm."

Jollos points out that failure to recognize such effects has led to much confusion in previous work on Protozoa, and he urges that in several of the cases mentioned above the so-called effects of selection were only "temporary modifications" that would have disappeared in time if selection were withdrawn or the environmental changes that were producing them were removed. In a word, that many of the cases of inheritance of acquired characters, so-called, produced by selection, or otherwise, are not comparable to the inheritance of characters that have arisen by mutation, which are permanent in that the germ-plasm itself has been affected. That mutational changes also may arise in the Protozoa in consequence of *changes in the environment during the conjugation period* is claimed by Jollos. His evidence shows, he believes, that mutations were induced both by arsenious acid and by high temperature. He states that there is a sensitive period at conjugation when mutations may be induced by environmental influences that do not affect the germ-plasm at other times. He is more doubtful as to whether such a sensitive stage is present during parthenogenesis (endomixis), but thinks that it may occur then also. Jollos distinguishes such effects from recombination changes in the germ-plasm, that may take place during conjugation, but how the distinction could be made manifest is not evident at all, for granting that

environmental changes affect the kind of recombinations that occur at conjugation, it would be almost impossible to show that one was not dealing with such effects, rather than with mutation.

It is not without interest in this connection to call attention again to the results of selection in a few of the higher plants where the basis of the selected differences rests on plastids present in the cytoplasm that multiply and transmit certain properties, independently of the hereditary complex contained in the nucleus. Here selection also produces immediate results that may also be reversed if not carried too far. Selection brings about effects that are strikingly like these described in the Protozoa, yet the mechanism in these same plants that gives in them Mendelian inheritance is not affected by selection of such "cytoplasmic" differences. There is certainly no contradiction here, but only two different processes each with its own mechanism, both of which are equally entitled to be called inheritance. Each of these kinds of heredity may play an important role within its own field, and in both the protozoa and the metazoa both kinds of inheritance may take place side by side. Such an interpretation leads then to the two following considerations:

First, it is thinkable at least, that selection in the Metazoa might sometimes involve the cytoplasm (and its inclusions) of the germ-cells themselves. If so, selection might bring about changes comparable to those described in the Protozoa. This might

take place independently of the mechanism of Mendelian heredity that applies only to genes carried by the chromosomes. All that need be said here is that as yet no evidence for such influence has been found.

Second, it remains to be shown whether in addition to this somatic selection in the Protozoa, if it be such, there may be another form of inheritance of the same kind as that prevalent in the Metazoa, based on differences in the chromatin of the protozoon individual. Let us now examine the evidence bearing on this question.

In the process of conjugation in the Protozoa there are phenomena that are often compared with those that occur in higher forms before and at the time of union of the sperm and egg. Whether previous to nuclear interchange there is reduction in the number of the hereditary elements and whether through interchange there are brought about recombinations of elements derived from the two parents are questions that can only be settled, as in the Metazoa, by a study of characteristics of parents (conjugants) and offspring.

Taking up first the mechanism, that of paramecium may serve for example (Figs. 70 and 71). During the time of fusion the macronucleus breaks up and its fragments are later absorbed. The micronucleus divides, and its daughter halves divide again, producing four micronuclei. Three of these are scattered in the protoplasm and disappear; one again divides into two. One of its halves passes into the other conjugant, and there unites with

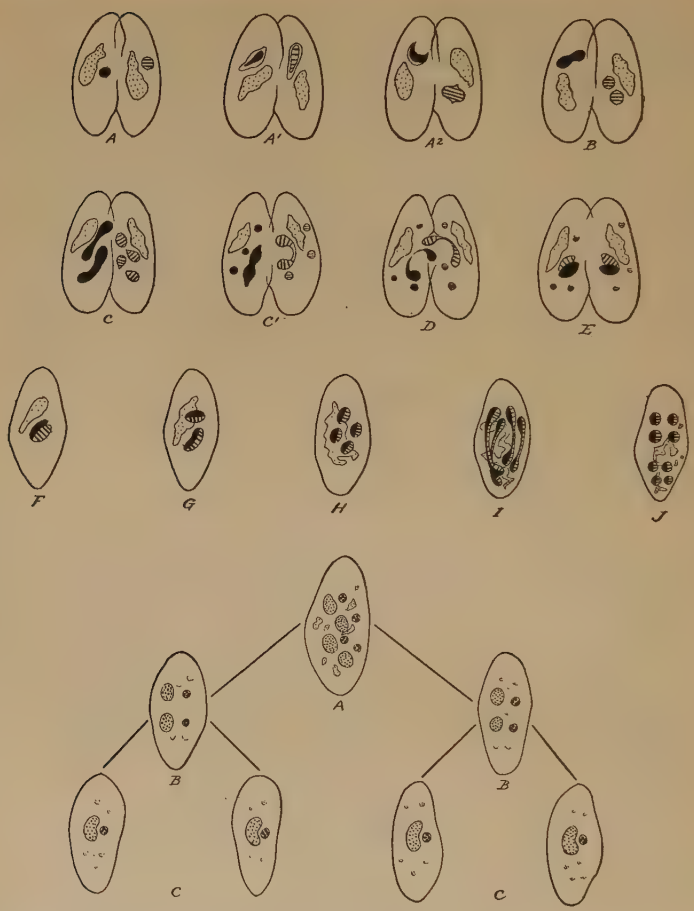


Fig. 70.—Conjugation process in Paramoecium, and the two peculiar divisions which follow it.

the one left in that individual. The exchange is reciprocal. The conjugants separate. In each there are three further divisions of the conjugant nucleus to produce eight micronuclei. In each individual

four of the nuclei enlarge to form macronuclei, four others remain as new micronuclei. Then the individual divides twice (Fig. 70). The macro-

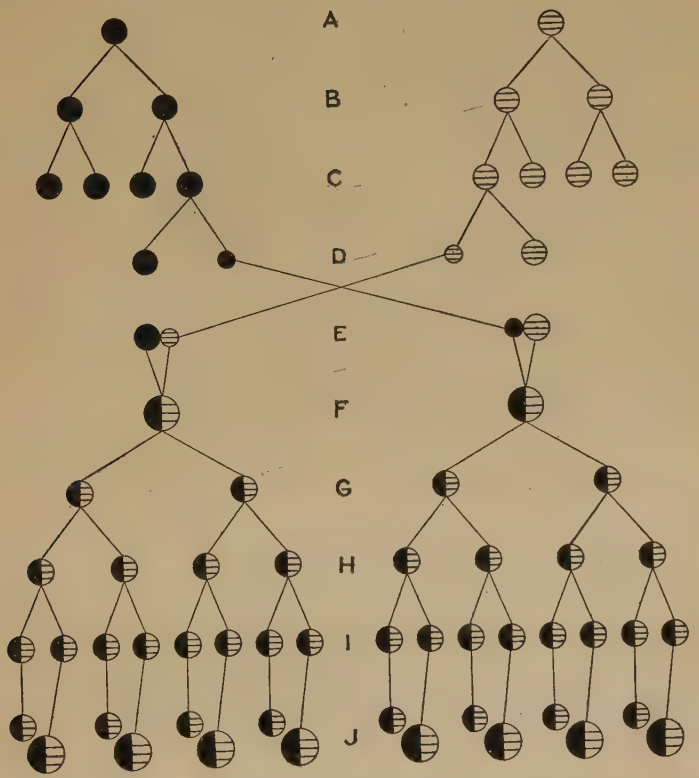


Fig. 71.—Diagram illustrating the history of the micronuclei in the conjugation and two subsequent divisions of Paramoecium.

nuclei and micronuclei do not divide at this time, but are distributed equally to each of the first two individuals, and then at the second division two go

to each of the resulting paramecia. Four lines of descent come from these four individuals from each ex-conjugant. Do the four different lines show differences, and do these differences bear any relation to the differences that existed in the original parents? In other words, are the two cell divisions, in which the products of the three divisions of the conjugated nuclei are sorted out, comparable, as has been suggested, to the two maturation divisions of the Metazoa? Calkins and Gregory have obtained results with Paramecium caudatum indicating that the four lines derived from each ex-conjugant may show different rates of division and different frequencies of conjugation-periods. This evidence seems at first sight to indicate that the two cell-divisions following conjugation may produce from the same material (conjugation nucleus) at least four different lines. If these results do not fall within the normal range of fluctuating variability, then it must be supposed that there occurs some process of sorting out of the elements (genes?) in the conjugated nucleus during its three consecutive divisions (in other words, segregation occurs), or else that imperfections and irregularities in the division either of the micronuclei or of the cytoplasm are introduced at this time. If the latter view were established one would expect that only some of the new lines would have a survival value if placed in competition. The remarkable fact that many of these lines soon die out even with the best attention, might possibly be appealed to as evidence

favorable to the view that the differences observed are in reality failures or imperfections in the processes taking place at this critical period.

This discussion is based on the assumption that reduction occurs after separation. If on the other hand, reduction of the chromosome number has taken place in the two parental individuals in the division immediately prior to interchange of micronuclei, then the two daughter individuals after interchange might be supposed to contain different hereditary complexes, but unless some further reduction takes place the four granddaughters from each ex-conjugant would be expected to give identical lines. In that case the evidence mentioned above would appear to prove too much, for only two different combinations are expected, not four or eight.

Something like reduction must occur somewhere if the chromosomes have the same values as in higher forms, for, if not, their number would steadily increase. An obvious objection to the hypothesis that the reduction occurs immediately *after* conjugation, is that it is purely speculative, for nothing peculiar in the division of the two micronuclei after conjugation has been observed. The divisions appear like ordinary divisions. Evidence as to whether the last nuclear division just *before* conjugation is reductional, or not, ought to be obtained from the history of so-called split-pairs. Jennings separated in many cases two individuals of the same line that were about to conjugate and recorded

their later rates of division. He compared their rates with the rates of sister individuals that were allowed to complete conjugation and then separate. He found that the split-pairs divide more rapidly than the ex-conjugants, and also that they show greater variation between the members of the pair than do the ex-conjugants. He interprets the result to mean that the ex-conjugants should be expected to be more alike in so far as they have each received a part of the other. This would only be expected, however, on the supposition that reduction did not take place at the last micronuclear division, *i.e.*, just previous to conjugation; for, if reduction had occurred then, the migrating nucleus of individual A, received by the mate B, would not, on the average, tend to be any more like the stationary nucleus of A than it is like either of the nuclei of B, and so the ex-conjugants would be no more alike than members of split-pairs. It may seem that a test as to whether any of the micronuclear divisions preceding conjugation are reductional might be made if the rate of division of the split-pairs were compared with that of the original strain from which they were derived. Jennings has made such a comparison and finds no difference between the rate of fission of the split-pairs and the rate of division of other individuals of the same culture that had not conjugated. This evidence appears to mean that no change in the hereditary complex takes place during the three micronuclear divisions preceding interchange; but this conclusion may

appear dubious until we know whether these divisions occur in the pairs which are split in the same way as in the conjugating individuals. It has also been shown by Woodruff and Erdmann that at intervals a process occurs in paramecium that they call endomixis, in which the individual undergoes changes that are like the first steps taken before conjugation. The old macronucleus breaks down and is absorbed. The micronucleus divides twice. Two of the four resulting nuclei disappear, one becomes the new micronucleus, and the other a new macronucleus. If reduction appears at this time, we should expect that sudden differences in the rate of division might appear. Erdmann finds positive evidence that supports this expectation. If the third micronuclear division, that does not appear in endomixis but does appear prior to conjugation, is the reduction division, then it may be difficult to reconcile such an interpretation with the comparison of the split-pairs that Jennings has made.

There is some evidence, in forms other than paramecium, showing that reduction in the number of chromosomes takes place prior to interchange. In the infusorian Didinium nasutum there are 16 chromosomes. In the first of the three maturation divisions of the micronuclei each daughter gets 16. In the second division the 16 separate into two groups of 8 each. In the third division each of the 8 divides giving 8 to each daughter. The full number would then be restored by conjugation.

In Uroleptis, Carchesium, Operculina, and Anoplo-

phrya, and in a few other forms, a similar reduction in the number of the chromosomes has been observed. It would seem more probable that we

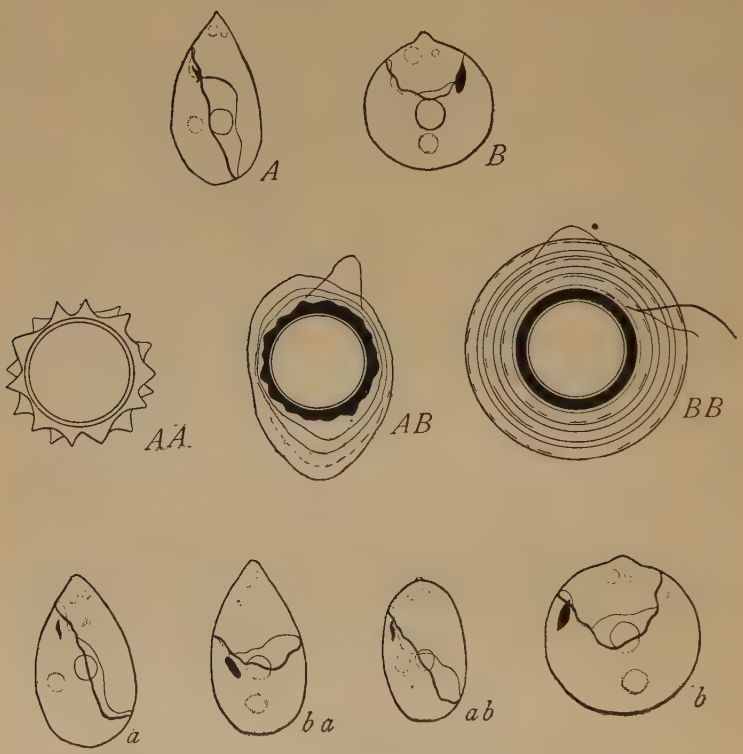


Fig. 72.—Two species of Chlamydomonas, *A* and *B*. *AA* and *BB*, conjugation cysts of *A* and *B* respectively. *AB*, hybrid cyst. *a*, *b*, *ba*, *ab*, types that develop from hybrid cysts. (After Pascher.)

must look for reduction before nuclear interchange rather than after that event. Even then it has by no means been shown that reduction here means segregation, as in the higher forms, for the value

of the individual chromosomes has not been demonstrated. There is, it is true, one case at least—in flagellates—in which the evidence seems to show that segregation takes place after conjugation. It has been shown by Pascher that when two species of Chlamydomonas conjugate and then encyst (Fig. 72) the resulting cyst is unlike the cyst of either parent, and may be said to be intermediate. While in the cyst, a reduction division occurs, and four new individuals emerge. These then multiply by fission. The offspring show the parental characters combined in different ways. Some of the individuals are like the parent species, others show recombinations of the original characters. The results, if confirmed, furnish evidence of segregation, but the numerical relations between the different types produced by each cyst are unknown.

CHAPTER XII

ŒNOTHERA AND THE MUTATION THEORY

The mutation theory was first developed by deVries on the basis of his extensive experiments with the Evening Primrose, Œnothera Lamarckiana. This plant was found growing wild at Hilversum, near Amsterdam, in Holland. DeVries noticed that several aberrant types were growing with the typical form, and when he planted in his garden self-fertilized seed from Lamarckiana (the typical form) he found that these other types reappeared in small numbers, and continued to do so year after year and generation after generation. Most of the new types themselves bred true with the exception that they also gave a few aberrant types in the same way as Lamarckiana. The following table shows the percentages of certain types obtained from Lamarckiana and from some of the new types themselves.

Soon after the rediscovery of Mendel's work (1900) the data that were rapidly collected regarding the genetic behavior of many different animals and plants made it evident that Œnothera was unique in its behavior in many other ways than in the relatively great frequency with which it produces new types. This led Bateson and Saunders,

New or "mutant" type	Frequency of appearance from different races						
	Lamarck-iana	lata	scin-tillans	simplex	nanella	oblonga	gigas
oblonga	0.7	0.7	6.1	0.0	0.02	.....	0.0
nanella	0.5	0.4	0.1	0.7	.....	0.0	0.9
lata	0.4	.....	0.4	0.3	0.02	0.0	0.0
scintillans	0.3	0.1	.....	0.3	0.0	0.0	0.0
albida	0.2	2.1	0.1	0.0	0.0	0.1	0.0
rubrinervis	0.04	0.2	0.0	0.0	0.0	0.2	0.0
ovata	0.01	0.4	0.0	0.0	0.0	0.0	0.0
deserens	0.0	0.0	0.0	3.2	0.0	0.0	0.0
metallica	0.0	0.0	0.0	1.5	0.0	0.0	0.0
Total new types	2.2	4.1	6.7	6.5	0.05	0.3	0.9

as early as 1902, to suggest that O. Lamarckiana might be a hybrid, and that the new types might be simply recombination products. There were very serious difficulties in the way of this hypothesis, and it was not strongly urged by its proponents. The view was, however, strengthened by a study of the history of the species. The members of the group to which it belongs are apparently all native in America, but several of them have become naturalized in Europe. It is very doubtful if O. Lamarckiana occurs in America as a wild plant, so that it may well be suspected of being a hybrid that was first obtained artificially and that then accidentally escaped and became established in Europe. Davis has worked on this hypothesis and has tried to synthesize the species by crossing wild American species. The question has now lost much of its point, however, through the discovery

by deVries, Stomps, and Bartlett that undoubted wild species of Œnothera show the same kind of behavior as Lamarckiana, and like it produce numerous new types.

The next suggestion as to the cause of the unusual behavior of Œnothera came with the discovery by Lutz that the "mutant" gigas has twice as many chromosomes as has the parent form, Lamarckiana (the diploid numbers being 28 and 14, respectively). The situation is complicated by the fact that there are apparently races that look like gigas but have only 14 chromosomes. These two races thus closely parallel the two giant races of Primula sinensis of which one is diploid and the other tetraploid. The aberrant numbers observed in gigas hybrids by Stomps may perhaps be due to a process of fragmentation of chromosomes similar to that described for O. scintillans by Hance.

Another type of variation in chromosome number has been described by Gates and by Lutz. The "mutant" types lata, semilata and scintillans have 15 chromosomes as the diploid number, instead of the 14 characteristic of Lamarckiana. As would have been expected if the extra chromosome is responsible for their peculiarities, these forms do not breed true. Each regularly produces many typical Lamarckiana offspring, as well as other offspring like itself. These cases have already been discussed under non-disjunction (see Chapter VI).

Although differences in chromosome number due to irregularities in reduction or fertilization may be

supposed to account for the types named, such differences do not offer an explanation of most of the other new types nor of the peculiar behavior shown by species crosses in the genus Œnothera. As will appear below these two classes of phenomena both suggest strongly that the plants are heterozygous, in spite of the fact that they breed nearly true.

If O. biennis and O. syrticola (muricata) are crossed, the F_1 hybrid strongly resembles the male parent, whichever way the cross is made. Combinations of these hybrids with each other and with both parent species have shown that the pollen and egg cells of each species carry different genes. The chief characteristics in which the two species differ are transmitted only through the pollen, and only the minor differences between the hybrids and their respective fathers are due to genes transmitted by the eggs.[1] The hybrids themselves behave in the same way so far as these characteristics are concerned; what they received from their father they transmit only through their pollen, what they received from their mother they transmit only through their eggs. As was pointed out by deVries, this phenomenon is perhaps to be connected with the fact, discovered in 1901 by Geerts, that about half the pollen grains and about half the ovules degenerate in certain of the Œnotheras—apparently

[1] These two species are quite similar, so that the characters transmitted in this peculiar fashion constitute only a small proportion of all the characters of the plants.

in all that show this peculiar behavior. It may be supposed that the eggs that contain the chromosome carrying the dominant genes distinguishing these species from each other all die, and that the pollen containing the chromosome that carries the recessive genes also dies. That is, we are dealing with a case of *gametic lethals*, the result of which is

Fig. 73.—Twin hybrids; *a*, Oenothera laeta, and *b*, Oenothera velutina. (After de Vries.)

to make the race in question breed constant though heterozygous.

When O. biennis, O. syrticola, or certain other species are fertilized by Lamarckiana or by certain of its "mutants" (*e.g.*, nanella, rubrinervis, or oblonga), the first generation hybrids are of two distinct types, called by deVries "læta" and "velutina." (Fig. 73.) This phenomenon was shown by deVries to be due to a peculiarity of Lamarckiana and

its derivatives rather than to the other species. An explanation was suggested in 1914 by Renner, who found that about half of the seeds of Lamarckiana fail to germinate. He supposed that the species was a permanent heterozygote for the læta-velutina pair of characters, which he treated as allelomorphs. The homozygous types were both assumed to be inviable, and to be represented by the seeds that fail to germinate. This view was at first opposed by deVries, but has since been adopted by him, and has been substantiated by so much evidence that it can now scarcely be doubted.

By 1917, then, the situation had been analyzed far enough to indicate that Œnothera Lamarckiana is a permanent heterozygote in at least two respects, and that its peculiar behavior in crosses is at least in part due to this heterozygosis. But in two respects the results were still unsatisfactory. No analogous case was known in any other organism, so that the hypotheses seemed curiously artificial and improbable; and there was no obvious relation between the heterozygous nature of O. Lamarckiana and the frequency with which it produces new types.

Both these objections were eliminated by the work of Muller on certain peculiar races of Drosophila. Muller examined the beaded race, which had long been a puzzle to those studying Drosophila. The beaded race, when first studied, did not breed true, but constantly produced normal flies. After a long period of selection, however, it began to breed almost true. In crosses the character

now appeared in about half the F_1 flies, never in all of them. Dexter had shown that the character was influenced by environmental and genetic modifying factors, and that the principal gene concerned was probably in the third chromosome. The fact that the stock had at first not bred true and then later had come to do so remained unexplained. Muller showed that the beaded factor itself is dominant, and that it is lethal when homozygous—*i.e.*, that the homozygous beaded individual dies. The stock had at first failed to breed true because all the beaded individuals were heterozygous for the normal allelomorph of beaded. But Muller also found that in the final stock there was a new lethal factor in the chromosome containing this normal allelomorph. The event that caused the stock to begin to breed true was evidently the mutation that produced this lethal. Crossing-over between the beaded factor and this lethal would ordinarily occur in a certain number of cases, but it so happened that in the non-beaded chromosome there was already present a factor that practically prevents crossing over in this region. The constitution of the individuals in the beaded stock then is as follows: $\frac{\text{Bd}}{\text{C}_{\text{III}}\ \text{l}_{\text{IIIa}}}$, where Bd represents the beaded factor, C_{III} the factor limiting crossing-over, and l_{IIIa} the lethal factor. The normal allelomorphs of these genes, present in the opposite chromosomes, have not been represented here. Such a "balanced lethal" stock not only breeds true though heterozygous, but parallels the

Œnothera situation in other respects. If this stock is crossed to wild type flies the F_1 individuals are beaded and wild-type in equal numbers, suggesting at once the "twin hybrids" (læta and velutina) of certain Œnothera crosses. If one of the "balanced" chromosomes contains one or more recessive mutant genes (and such have been purposely introduced into it by appropriate crosses), crossing over between any of the recessive genes and the lethal region may cause the appearance of a small number of specimens showing the corresponding recessive characters, and these will be produced in small numbers generation after generation, exactly as in the case of such "mutants" of O. Lamarckiana as nanella or oblonga. The frequency with which these types will appear will depend simply on the frequency with which crossing over occurs—*i.e.*, on the loci of the genes in question.

Similar cases of balanced lethals have since been observed in other races of D. melanogaster, such as truncate and certain races of dichæte. In at least one instance such a race has been artificially made up in order to save labor in keeping stock of certain lethal characters. There are strong indications that a somewhat similar case of balanced lethals occurs in stocks (Matthiola).

This work of Muller's, then, furnished definite information that permanent heterozygotes due to balanced lethals can and do exist, and furthermore correlated this phenomenon with the repeated appearance of apparently new types in small numbers.

An application of the principle of balanced lethals to O. Lamarckiana indicates that the chromosome pair that contains the balanced zygotic lethals (*i.e.*, that is responsible for the differences between læta and velutina) is the one that is most important in the production of the "mutant" types. It is apparently in this pair of chromosomes that nanella, oblonga, rubrinervis, blandina, simplex, erythrina, and others differ from typical Lamarckiana. If we regard Lamarckiana itself as heterozygous and write its formula $\frac{\text{læta}}{\text{velutina}}$ it is possible to write similar formulæ for the other types named, as has been done in a slightly different fashion by deVries himself. The "læta" and "velutina" are not to be thought of as single allelomorphs, but rather as whole homologous chromosomes that differ in a number of genes. In the formulæ below the other terms may be thought of as follows:

oblonga — mostly læta, but modified either by crossing over or by mutation.
deserens — like læta in most respects.
decipiens — also like læta. Differs from deserens only in not having a gene for brittleness.
blandina — smooth leaved; otherwise like velutina.

None of these, except oblonga, carries a lethal; the lethals have presumably been lost by crossing over.

The terms just given apply to the chromosomes; the plants themselves may be represented as follows:

$$\text{oblonga} = \frac{\text{oblonga}}{\text{velutina}} \qquad \text{rubrinervis} = \frac{\text{deserens}}{\text{velutina}}$$

$$\text{lucida} = \frac{\text{deserens}}{\text{læta}} \text{ or } \frac{\text{decipiens}}{\text{læta}}$$

$$\text{deserens} = \frac{\text{deserens}}{\text{deserens}} \qquad \text{erythrina} = \frac{\text{decipiens}}{\text{velutina}}$$

$$\text{decipiens} = \frac{\text{decipiens}}{\text{decipiens}} \qquad \text{blandina} = \frac{\text{blandina}}{\text{blandina}}$$

$$\text{simplex} = \frac{\text{læta (minus the lethal)}}{\text{læta}}$$

There is apparently normally a gene for dwarfness in the læta chromosome, and the appearance of nanella is due to this gene crossing over from most of the rest of the complex to give a chromosome that is velutina plus dwarfness. This chromosome, if at fertilization it enters the same zygote as a normal læta chromosome, will give rise to a dwarf that is still in the balanced lethal condition and that will react in most respects like Lamarckiana itself.

It seems very probable that the differences between most of the chromosomes in these mutant types are due to their being the results of crossing over at different levels. They are simply mixtures of the original læta and velutina chromosomes in different proportions. DeVries, however, believes that all of the differences between them are due to mutation rather than to crossing over, and it may well be that some of them are of this nature. It is not yet possible to construct a map of this chromosome that will explain the observed results consistently. Shull has recently given a preliminary

report of experiments on the crossing over value for some of the factors in this chromosome.

The interpretation just given will account for a large proportion of the results reported by deVries and others; but there still remain certain curious facts that do not fall into line. There are some other unusual factors that have not yet been taken into account. Nevertheless, it is evident that Œnothera will not long remain as the one outstanding case that cannot be brought into line with other genetic phenomena.

It is evident from what has been said that Œnothera is not a favorable object for the study of the manner and frequency of occurrence of new mutations in the germ plasm. We require for such a study an organism the normal genetic behavior of which is thoroughly understood, and one that is not normally heterozygous for an unknown number of little understood genes. Yet it was deVries' experiments with Œnothera that first drew attention to mutation, and the whole history of the mutation theory is bound up with Œnothera. These facts have led certain authors to attack the mutation theory and to proclaim its downfall. Lotsy, for example, maintains that mutations do not occur and that all evolution is due to hybridization and recombination. The Œnotheras do furnish conclusive evidence that new types may appear suddenly and without the occurrence of intermediates. It was this phenomenon that deVries originally termed mutation. Nowadays we use the term mutation

to indicate a change in the nature of some part of the germ-plasm; and the peculiar behavior of Œnothera makes it very unfavorable for the study of this phenomenon, or for the proof of its occurrence. Fortunately, however, there is abundant evidence that mutations in the germ-plasm do occur in other forms, where they cannot possibly be explained as recombination products.

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